UNIVERSITY OF TORONTO
3 1761 01046125 9

Digitized by the Internet Archive
in 2019 with funding from
University of Toronto

https://archive.org/details/animalexperiment00spen

87
518

ANIMAL EXPERIMENTS AND SURGERY

NIMAL EXPERIMENTS
AND SURGERY

HUNTERIAN LECTURES
delivered at the Royal College of Surgeons of England
on February 13, 16 and 18, 1920.

BY

eorge
WALTER G. SPENCER, M.S., F.R.C.S.

SURGEON TO THE WESTMINSTER HOSPITAL; MEMBER OF COUNCIL AND
LATE MEMBER OF THE COURT OF EXAMINERS OF THE ROYAL
COLLEGE OF SURGEONS OF ENGLAND; ALSO LATE
EXAMINER IN SURGERY AT THE UNIVERSITIES
OF LONDON AND MANCHESTER

20942
23.2.27

LONDON
UNIVERSITY OF LONDON PRESS, LTD.
18 WARWICK SQUARE, E.C. 4

1920

RD
29
S64

INTRODUCTION

In the summer of 1918, a Bill was laid before Parliament to prevent experiments on dogs which it became necessary to defeat. Sir Charles Ballance and I thought that we could help in this by explaining the intimate connection between Surgery and Animal Experimentation. We sent some letters to *The Times*, on which we received so much commendation and so many expressions of approval, that it has led me to set out in a fuller way what was briefly summarised in the letters.

Before beginning to do so I make two observations which have reference to the subject as a whole.

Opposition to the advance of Medical Knowledge by means of Experiments on Animals has been met and countered, very ably, by physiologists both here and in the United States. I exhibit four books from the Library of the College as examples.

The Hon. Secretary of the Research Defence Society, Mr. Stephen Paget, published in 1906 his *Experiments on Animals*, with a Preface by Lord Lister.

Dr. W. W. Keen of Philadelphia published in 1914 his *Animal Experimentation and Medical Progress*, with a Preface by Dr. C. W. Elliot, President Emeritus of Harvard University.

The other two books were written by Michael Foster, viz. his *Lectures on the History of Physiology in the Sixteenth, Seventeenth and Eighteenth Centuries*, and his *Life of Claude Bernard.*

The second general statement refers to that which opponents of Experimentation continually affect to ignore, viz. the evidence that discoveries concerning antisepsis and anæsthesia, general and local, have established a regular practice of preventing pain, just as much when experimenting on animals as when operating on man.

In the selections from the history of surgery which I make, my aim is to associate a definite advance in surgery with the experiments on animals which directed that advance.

These selections are grouped under three heads :—

(1) An account in historical sequence of some of the Experiments which have had a principal influence upon the Development of Surgery.

(2) A description of Experiments which directed the application of Surgery to the Organs and Organised Structures of the deeper parts of the body.

(3) An explanation of how discoveries made by Experiments have enabled the scope of parts of Surgery to be extended indefinitely.

On the other hand, some of these discoveries have resulted in Improvements in medical treatment, and have rendered unnecessary much of what was indifferent surgical treatment.

CONTENTS

PAGE
INTRODUCTION v

I

AN ACCOUNT IN HISTORICAL SEQUENCE . . . 1
Roman Veterinary Surgery. Homer and Wounds . 2
Galen—Experiments relating to Surgery . . . 9
Vesalius—Experiments supplementary to Anatomical Instruction 25
Discoveries in Italy—Zambeccari 32
The spread from Italy to the North. Von Haller . 34
The Académie de Chirurgie 37
The *Philosophical Transactions* 38
The Hunters, Astley Cooper, and their Contemporaries 42
The Nineteenth Century in France, Germany, the United States and this country 47
The Attaining of Manual Skill 51

II

THE APPLICATION OF SURGERY TO ORGANS AND ORGANISED STRUCTURES 54
Transfusion of Blood and Infusion of Fluids . . 54
Ligature and Suture of Arteries—Suture of Wounds of the Heart 61
Asphyxia and Artificial Respiration—Apnœa . . 77
Intestinal Suture and Anastomosis—Intestinal Obstruction 87
Gastric and Biliary Surgery. Surgery of the Spleen and Pancreas 94

III

IMPROVEMENTS IN SURGERY 108
    The Nervous System 108
    Thyroid and Renal Surgery 126
    Septic Organisms 132
    Anthrax, Rabies, Diphtheria, Tetanus and Venereal Disease 141
    Conclusion 164
REFERENCES 166

ANIMAL EXPERIMENTS AND SURGERY

I

AN ACCOUNT IN HISTORICAL SEQUENCE OF SOME OF THE EXPERIMENTS WHICH HAVE HAD A PRINCIPAL INFLUENCE UPON THE DEVELOPMENT OF SURGERY

If I describe experiments made in bygone days, it is for the purpose of demonstrating continuity. The experiment directed a definite advance in surgery; therefore by recalling the past I aim to establish the conviction that experiments on animals will point the way to surgeons in the future.

Now the results of experiments have been often neglected by practical surgeons—Galen's experiments relating to surgery were not appreciated for 1800 years, others for a century or two, more or less, and I shall be able to point to three recent instances. At the beginning of the late War there existed published accounts of experiments on transfusion, tetanus and excision of infected wounds, the bearings of which were not fully grasped. At varying periods after the commencement of the War, improvements in surgery occurred, which might have been begun earlier had more attention been paid to the results of experimental work.

Roman Veterinary Surgery

Surgery originated in prehistoric times in a way which can only be a matter of conjecture, but it must have been closely connected with the operations done upon domesticated animals. That was the opinion of the Roman writer Celsus, for in his opening sentence he allied the Art of Medicine with that of Agriculture. Alongside the practice of medicine the Romans had developed veterinary medicine and surgery which was practised on the large estates and farms. The earliest writer on veterinary medicine and surgery was Mago the Carthaginian (*c.* 200 B.C.), then Varro (116–26 B.C.), Columella (*c.* A.D. 40), and later Vegetius (A.D. 450–510), who copied from his predecessors. Stone was removed from a horse's bladder through the rectum, by the aid of a calculus hook mentioned by Celsus. Cataracts in the eyes of horses caused by flicks of the whip, the eyes not being protected by blinkers, were couched by paracentesis; enlarged submaxillary glands were excised; suppuration in the parotid region and neck causing strangles was incised; nasal polypi were removed; venesection from the external jugular vein, also from the vein of the septum nasi, was frequently used.

The castration of animals was a most ancient practice, as proved by the special names for the gelding and ox. The methods of crushing, cutting out and tearing out were referred to by Moses. The various methods in use down to the present have been evolved by long experience, which has devised safe methods. No method would have become established unless it could be carried out with only a small loss of young animals. In the course of castrating was learnt the correct use of the cautery at a dull red heat so as to sear but not to char. The curious method called bistournage demanded skill and long experience. Another remarkable instance of combined skill and experience was the old Chinese method of castrating cockerels singlehanded, the bird being held to the ground by the bare foot. The operation for the cure of hernia, as described by Celsus, was similar to that of castrating by transfixing the cord with a ligature.

Homer and Wounds

A book often quoted by ancient medical writers is the *Iliad* of Homer, because there is contained in it descriptions of more than 150 wounds, over two-thirds fatal. What is remarkable is that the account of the wounds and wounding is a natural one, within the bounds of what may possibly have happened. In this respect there is a great difference from the description of injuries in subsequent romance writers down to the present day. Observations made during and after fighting do not afford a sufficient explanation; the writer of the *Iliad* appears to have combined the experience of a warrior with that of a hunter who knew where to strike a deer, also how to slaughter a horse or ox, and the effect of decapitating a sheep or goat for sacrifice.

The following are some of the noteworthy descriptions:—

The *deadly spot on a horse's forehead.* (*Il.*, VIII. 80–86.)

" But his horse was done for, which Alexander had smitten with an arrow upon the top of the forehead where the front hairs of horses grow from the skull; and there is the most deadly mark. So the horse reared in anguish as the arrow plunged into the brain, and as he rolled over with the arrow, he dragged down his fellow-horses." The spot is that which is struck with the pole-axe.

An *ox slaughtered by a stroke between the occiput and atlas.* (*Il.*, XVII. 520.)

"As when a strong man with a sharp axe cuts behind the horns of a working ox right through the sinew (the ligamentum nuchæ), the ox leaps forward and falls." Galen referred to this method as used in sacrificing oxen at the temples and attributed the instantaneous death to the wounding of the fourth ventricle.

Fracture of the cervical vertebræ. (*Il.*, V. 154–164.)

"Then Diomedes caught the two sons of Priam the Dardamian as they rode together in a chariot, Echemmon and Chromios. As a lion among cattle in a woodland pasture leaping upon a cow or heifer breaks the neck, so the son of Tydeus thrust them both, in spite of their resistance, out of the chariot to their death, and thereafter despoiled them of their arms."

A lion has been often observed to break the neck without using his teeth; the lion, as it were, causes the frightened beast to break its own neck. This passage shows plainly that the knowledge of what a lion does was transferred to human fighting.

A wound of the heart as shown by the movement of the butt end of the spear, the point of which had penetrated the heart. (*Il.*, XIII. 439–443.)

"And he fell with a crash and the lance fixed in the heart, that, still beating, shook the butt end of the spear."

A hunter might well have observed this when giving the finishing stroke to a deer held at bay. The passage suggested the earlier experiments on the heart. In human beings the sign has been noted, *e. g.* when a woman knitting whilst walking, has stumbled and a knitting needle has penetrated the chest.

Decapitation

"Diomedes smote Dolon, as he was bending forwards to beg for quarter, on the nape of the neck and cut through both sinews (*e. g.* on each side of the spine), and the head of him still speaking was mingled with the dust" (*Il.*, X. 457).

"Therewith Odysseus caught up a sword in his strong hand and drove it through the neck of Agelaus, who was kneeling and begging for mercy, whose head as he yet spake fell even to the dust" (*Od.*, XXII. 329).

"Ajax cut off the head of Imbrios from his delicate neck, and sent it rolling like a ball through the throng, and it dropped in the dust before the feet of Hector" (*Il.*, XIII. 200).

"And Achilles smiting the neck of Deukalion with his sword, swept off both head and helmet, and the marrow rose out of the spine, and he lay as a corpse stretched out upon the ground" (*Il.*, XX. 480–483).

"The spear struck Archelochos at the junction of the head and neck, on the top vertebra, cutting through the sinews, and his head, mouth and nose, as he fell, reached the earth long before his legs and knees" (*Il.*, XIV. 465–468).

These descriptions suggest observations perhaps on men being executed, but also on animals, sheep and goats when sacrificed. Aristotle (*Parts of Animals*, III. 10), discussing the above passages and the possibility of a decapitated head speaking, said that in the course of a trial for murder in Caria, the murdered man's head, after it had been severed from his body, was asserted to have repeated several times the words, "Cercidas slew man on man." Hence a man named Cercidas was arrested and put on trial.

Le Gallois in 1812 was the first to explain by his experiments the inarticulate death shriek and the snapping of the jaws. He said that there had been incidents at the guillotining of aristocrats. The head of one as it fell to the scaffold had spoken last words to his friends; another had wreaked last vengeance by biting the executioner's toe; a third had turned up his eyes in a last long look at his relations. A convulsive spasm of the muscles producing the voice, closing the jaws and moving the eyes is the cause of the phenomena. The protrusion of the spinal marrow is due to a general convulsion of the muscles of the trunk.

Wound of the Bladder through the Buttock. (*Il.*, XIII. 650–655.)

"But Meriones shot at Harpalion as he retreated with a bronze-shod arrow, and hit him in the right buttock, and the arrow going right through the bladder came out under the (unnamed) bone. And sitting down, even there, in the arms of his dear comrades, he breathed away his soul, lying stretched like a worm on the ground, and out flowed the black blood and wetted the ground." Also—

"Meriones pursued Phereklos and, overtaking him, smote him in the right buttock, and right through straight to the bladder passed the point beneath the (unnamed) bone; and he fell to his knees with a cry, and death overshadowed him" (*Il.*, V. 65–68).

There was then no acquaintance with human anatomy, but a hunter would know the stroke, for as the spear penetrated it would at the same time injure the sciatic nerve and paralyse the animal's leg. Galen stereotyped the term "the innominate bone."

Galen's Experiments relating to Surgery

Galen is generally known because in his works are contained an account of the anatomy, physiology and medical philosophy of the Greek and Roman world. Except for the so-called works of Hippocrates and Celsus, all else before is lost. Perhaps Galen's MSS. were copied by monks and preserved until the era of printing, because he was a pious monotheist, continually using the Argument from Design, in which he was copied by the authors of the Bridgewater Treatises early in the last century. How much he copied from his predecessors on anatomy and physiology is a matter of conjecture. But his experiments were his own. References to experiments are scattered throughout his works, but they are chiefly met with in his *Anatomical Administrations* or *Dissector's Manual*. The last seven books of this treatise are not extant in Greek and Latin; they are preserved only in an Arabic translation. There is one MS. at Oxford and another in the British Museum. A translation into English was made by W. A. Greenhill, but it has not been published. I have taken my statements from Max. Simon's German translation in 1906. His first volume reproduces the Arabic Text with Notes; his second volume contains the German translation, with Commentary and Notes.

Galen seems to have described his experiments in the Greek language to audiences in Rome composed not only of medical practitioners but also of the general public. They read as if what he said was taken down at the time by an amanuensis and not afterwards rewritten. There is much repetition and an enormous emphasis on definition.

Now upon whatever else the fame of Galen rests, he commenced practice as a surgeon, and he is the first on record to make systematic experiments on animals with the object of throwing light on surgical questions. He took a keen interest in the mistakes made by Roman surgeons, and their mistakes suggested to him some of his experiments. To have carried them out he must have been a most skilful operator.

Galen, at the age of twenty-eight, after a long course of study and travel, commenced practice as a surgeon to the palæstra in his native town of Pergamos. Not only did this involve the treatment of injuries resulting from wrestling and boxing, but also of the wounds received by the gladiators in their combats. One of Galen's chief writings at a later date was his commentary on the treatises included in the works of Hippocrates concerning fracture, dislocation and sprain, which occur especially in the course of wrestling and boxing, and which had been written 500 years before Galen's time by some surgeon whose special experience had been gained in the palæstra in the same country, Ionia. When Galen, after four years, moved to Rome, he was not allowed to practise surgery as well as medicine, but he was frequently called into consultation over surgical cases.

The Recurrent Laryngeal Nerves

A chain of experiments was started by two cases in which surgeons had injured the recurrent laryngeal nerves; deep-seated glands in the neck were being shelled out, the finger-nail being used to scratch through the capsule. In one child both nerves were injured, with complete loss of voice; in the other only one side was injured. The term used, viz. *Choirades,* Daremberg translated *goitres,* and it is difficult to understand how recurrent laryngeal nerves could be injured on both sides unless it was a thyroid gland tumour which was being shelled out. Now Aristotle was understood to have taught that the voice was produced in the lungs and windpipe. "Every one wondered," said Galen, "that the voice was found impaired. When I demonstrated the nerves of voice, their wonderment ceased." The experiments were best done on pigs or goats, which readily use their voice and have not the repellent aspect of the ape; also birds with long necks such as cranes, swans and the ostrich were suitable. The nerves were divided, or, being compressed by a temporary ligature, when this was relaxed, the voice returned. Galen, using a thin pig and pulling on the nerve, traced it on the right side round the subclavian artery and round the aorta on the left. It was the idea of Galen that the action of the nerve was like the cord of a bell running over a pulley, and so it was an illustration of reflected motion. When he jerked the nerve, muscles belonging to the larynx twitched.

An analogy was furnished by a racecourse with a turning-post, beyond which the runner returns on his track, and hence the name the nerves have always borne (Gr. *Neura palindromounta*, Lat. *Nervi recurrentes*).

Having followed the recurrent nerves to their end by dissection, Galen proceeded to examine the movements of the laryngeal muscles in animals. He rightly described the crico-arytenoidei postici as openers of the larynx. The thyro-arytenoidei, in which he included both the true and false vocal cords, were the closers of the glottis.

These experiments and observations on the recurrent laryngeal nerves attained importance after the middle of the nineteenth century when the surgical treatment of goitre was commenced, and when the invention of the laryngoscope allowed the interior of the larynx and its movements to be inspected.

Ligature of the Carotids

Galen's opponents objected that the loss of voice was due to ligature of the carotid arteries. The compression of the carotids in the neck was known to produce unconsciousness; and the name carotid was derived from *karos*, deep sleep. In the East, compression of the carotids had been used from ancient times for producing unconsciousness when circumcising boys. Galen tied both carotids in dogs without causing loss of voice, and he affirmed that the loss of voice following that experiment by others had been due to the inclusion of the vagus nerves in the ligatures.

THE ARTERIES AND HÆMORRHAGE

Galen's experiments on the ligature of large arteries like the carotid brought him to the point of demonstrating that the blood flows through the arteries in one way only, viz. from the heart. But he confined himself to confuting the statement attributed to Erasistratos that arteries contained only air when unwounded. To explain arterial bleeding from a wound, Erasistratos had assumed that as a result of the injury anastomoses between veins and arteries, otherwise closed, were opened up. Galen placed two ligatures upon an artery and made an incision into the artery between the ligatures, when the artery was found full of blood. Also having exposed a large artery, he made a longitudinal incision into it and slipped into the lumen a hollow reed or bronze cannula. Then he closed the incision. It was thus demonstrated that the pulse in the artery beyond the cannula continued as before, until a ligature placed round the artery above the cannula was tightened, when pulsation beyond the cannula ceased. By puncturing arteries he showed that bright blood, not air, escaped.

From these experiments Galen drew the practical conclusion that to arrest bleeding from a wounded artery, the ligature must be applied to what he called the roots of the artery, *i. e.* between the wound in the artery and the heart.

Exposure of the Heart

Galen's surgical skill enabled him to expose the heart in a young pig without opening either pleural cavity. He was able to handle the heart whilst the animal continued to breathe spontaneously and to cry. After closing and bandaging the wound, the animal was released; it then ran about, ate and drank. When he attempted to apply a ligature to the pulmonary artery, the pleural cavity was opened and the animal died of asphyxia. To the experience gained by these experiments Galen attributed his success in removing a necrosed sternum—an operation he often referred to. Although he failed to discover that the blood circulates, his experiments in the end became the starting-point for the successful application of surgery to relieve wounds of the heart.

The Intercostal Muscles and the Ribs

Galen made another series of experiments to show that the voice was not produced by the lungs. In the course of these experiments he discovered the actions of the intercostal muscles, and he gave a precise description of the method of excising a rib, without opening the pleural cavity. The following is his description :—

“ When the animal breathes forcibly or cries, the outline of a rib can be distinguished from the adjacent intercostal spaces. This done, the skin and soft parts are cut through with a knife, whether by one or more strokes. But care must be taken that the knife does not slip off the convexity of the rib, for along the under border of each rib there is not only a nerve but an artery and vein as well. The quicker the cut is made the better. Now each rib is enclosed, both on its convex and on its concave aspect by a membrane, just like other periosteal membranes. This is cut through in the long axis of the rib, and is then separated from the bone by using a myrtle-leaf-shaped raspatory, curved at both ends. When thus detached so as to expose enough bone, a fine meninges guard or a broad flat probe is inserted between the raised periosteum and the bared rib, taking care not to tear or perforate the membrane. This done, the rib is cut through in the usual way, by two chisels applied the one opposite the other.” There were then no shears which would cut through ribs.

After Lister’s introduction of antiseptic surgery the opening of pleural empyema came to be generally practised, and then the method of excising a portion of rib as described by Galen was followed.

THE SPINAL CORD

For his experiments on the spinal cord, Galen employed monkeys, also young pigs in which he was able to cut through the spines and laminæ with a strong knife. In monkeys he passed a fine, flat-bladed knife between the laminæ, so as to cut across the cord transversely. In order to divide the spinal cord longitudinally, after removing spines and laminæ, he raised the dura mater on a hook so as to incise it without wounding the pia mater. He could then cut the cord exactly along the middle line with a fine knife; there was no disturbance of function, neither the intercostal nerves nor the nerves passing to the hind limbs were paralysed.

When the cord was divided transversely, the nerves connected with the spinal cord below the level of division lost the function both of sensation and of motion. If the transverse section was made at the level of the sacrum, sensation and motion were lost in the foot, and as the section was made higher up, so there was loss of sensation and of motion in the thigh, the hip and lumbar region. When the transverse section was made at the level of the thoracic vertebræ, the forcible respiratory movements of the animal began to weaken. When the section was made just below the middle of the dorsal region, movement continued in the upper intercostals, the upper accessory muscles of respiration and the diaphragm. Galen also noticed that the serratus posticus inferior has a high nerve supply, an observation only confirmed in recent years.

In monkeys, so long as the section was below the second intercostal space, power in the arms was preserved. A section just above this level caused loss of sensation in the skin of the axilla and inner side of the arms, *i. e.* in the distribution of the intercosto-humeral nerves. The hands of the monkey were weakened when the section was made at the level of the first rib. When the section was between the seventh and eighth cervical vertebræ, the forearms were weakened but the action of the accessory muscles of respiration continued. By a section at the level of the fifth cervical vertebra the arms were completely paralysed; the diaphragm continued in full movement, also the scaleni, whilst all the intercostal movement was lost.

In sacrificing an ox at a temple, a puncture was made behind between the skull and the first vertebra, then all four limbs were rendered powerless at once and the breathing was arrested. This, said Galen, was due to a penetrating injury of the fourth ventricle. The same result followed division of the spinal cord between the second, third and fourth cervical vertebræ, provided that in the last section the nerves between the fourth and fifth vertebræ were cut, for the nerves to the diaphragm made their exit by them.

Galen exhibited marvellous skill and acumen in his experiments on the spinal cord, the importance of which only became evident in the nineteenth century. Then further additions were made by Le Gallois' experiments on the respiratory centre in the medulla, by Charles Bell's observations on injuries to the spinal cord in man, and by Magendie's demonstrations of the spinal roots. Later in the century Galen's experiments received further confirmation by the demonstration that the spinal cord was not a mere bundle of nerves, but that in it could be distinguished different centres and tracts. His experiments are the foundations upon which the application of surgery to the spinal cord is based. If after injecting a dose of stovain into the lower part of the spinal theca, the patient's head and trunk are placed too low, it can be noted that the intercostal muscles become paralysed from below upwards; then the patient will lose sensation on the inner side of the arm, next the hands will become numbed and weakened.

Experiments on the Brain

After giving a description of the dissection of the brain in a dead animal, Galen proceeded to describe the experiments he had carried out on a living pig, goat and monkey. With all care the skull was trephined so as to expose the dura mater uninjured. Then the brain could be seen under the meninges to rise and sink alternatively, by a pulsation resembling that of the arteries. The space between the dura mater and pia mater permitted of the movement. Whilst some held that the movement was inherent in the brain, others in the meninges, Galen said that it was due to the arteries. When opening the dura, it was necessary to keep the brain warm or it would become chilled and irresponsive.

When pressure was made on the brain over the lateral ventricles, there was slight benumbing of the animal. When the brain overlying the third ventricle was compressed, the animal was more deeply numbed; this became more marked when the cerebellum was pressed down upon the fourth ventricle. Pressure made in the neighbourhood of the optic nerves caused the animal to show ocular disturbance.

Experiments on compression of the brain were resumed in the nineteenth century, and have served as guides to the surgeon in relieving the effects of intracranial tension.

EXPERIMENTS ON MUSCLES

The œsophagus was first examined in a dead animal and found to be composed of muscle continuous with the stomach, the inner layer of longitudinal, the outer of circular fibres.

On a living animal the outer circular fibres were divided by a longitudinal incision, when the wound having been closed by suture, and the animal being hungry and thirsty, it swallowed. By means of a transverse incision between the circular fibres, the longitudinal fibres were divided, when the animal could also swallow. Thus he showed that the longitudinal and circular fibres acted together; only one of the two layers of fibres were essential for swallowing, although that movement was then weaker than normal.

Experiments on the muscles of the limbs were suggested by the necessity often arising of cutting muscles when opening deep abscesses. When a large muscle was cut across, the divided parts retracted and the muscle lost its special energy, so that its particular function was abolished. A knowledge of the particular function of each deep muscle was necessary to a surgeon. A gladiator received a large wound, by which the muscles of the front of the thigh were cut across. Galen exposed freely the divided ends and drew them together by sutures, and in this way the function of the muscles was regained. His experiments gave rise to his description of what he called "opposites," *i. e.* of muscles antagonising one another. The division of a muscle or its tendon caused the drawing over by the antagonist muscles, but in doing this an antagonising muscle showed a diminution in its power of contraction. This Galen explained was due to the fact that any contraction of muscle requires, as a preliminary, tension on the part of the opposite muscle. He demonstrated this by dividing a flexor muscle of the arm and then bending the elbow; when let go the limb was extended, but more feebly than natural. By studying muscles separately, he noted for each its special function, and upon this he based his peculiar nomenclature of the muscles. He demonstrated for each muscle that for action it possesses tenseness and contractibility, while its antagonist develops an active faculty of stretching and relaxing. The activity of muscles, which he termed tonic action, he instanced by the state of the muscles when the arm was held elevated, although the limb was apparently motionless. There was a further force required to set in action, now one muscle, now another. This was the psychic tonus or psychic force emanating from the brain.

To give one instance showing Galen's methods of discovering the function of muscles, he cut the trapezius horizontally across the neck; the scapula was then drawn down and could not be lifted up. The same result followed from the division of the spinal accessory nerve.

Nothing is more remarkable in Galen's experimental researches than those on muscles. He aimed to solve questions which are of importance at the present time, *e.g.* in connection with the treatment of wounded muscles and nerves.

EXPERIMENTS ON THE URETER

Galen in his *Anatomical Administration*, VI. 13, and on the *Natural Faculties*, I. 13, said that Asklepiades had put forward the absurd view that the bladder soaked up urinous vapour from the rest of the body like a sponge. Every butcher, however, observed daily the position of the kidney and of its duct, called the ureter, leading into the bladder. All sufferers from dysuria and ischuria, when they feel pain in the loins (*psoai*) and pass sandy matters in the urine, call themselves nephritics, *i. e.* sufferers from kidney troubles. Asklepiades could never have watched a patient passing a stone; the sharp pain, beginning in the kidneys, passed down the ureter to the bladder, when both the pain and the ischuria stopped. One of the Asklepideans had attempted to contest Galen's argument by tying up the neck of an ox bladder, after filling it with water. When squeezed, fluid did not escape backwards up the ureters.

Galen demonstrated that when the bladder was laid open in a living animal urine was seen to be continually flowing from the orifices of the ureters into the bladder. He then exposed the ureter on each side and applied a ligature. The animal being bandaged up and let go did not urinate. On taking off the bandage the bladder was found empty, but the ureters above the ligatures distended almost to the point of rupturing. On removing the ligatures the bladder filled with urine. When the urethra of an animal was tied, the bladder filled, but none regurgitated up the ureters, not even when the full bladder was squeezed. Thus the absence of regurgitation was demonstrated in the living. If one ureter was tied, it became distended above the ligature, whilst the opposite ureter continued to conduct urine into the bladder. On puncturing the distended ureter urine spurted out as does blood from the vein in venesection. Both ureters being cut across through the peritoneal cavity, the bladder remained empty, but the peritoneal cavity filled with urine, as if the animal were suffering from dropsy.

The prevention of regurgitation is the great means of protecting the kidneys from becoming infected from below, and this was his discovery.

VESALIUS SUPPLEMENTED ANATOMICAL INSTRUCTION

Vesalius in 1543, in the final chapter of his *De humani corporis fabrica,* described how he had supplemented his Anatomical Instruction by experiments on animals. In the frontispiece, in which Vesalius is depicted himself acting at once as both dissector and demonstrator on a cadaver, to a large and mixed audience, a servant is holding a monkey in readiness to supplement the demonstration. Also in the thumbnail sketches used as vignettes for the capital letter, he has poked fun at his medical students, drawing them as cupids, among other things experimenting on and dissecting dogs and young pigs.

The chapter contains a systematised account of Galen's experiments, together with additions by Vesalius himself, directed towards the teaching of anatomy, physiology and surgery. The chapter contains instruction upon experimental physiology and experimental pathology, as well as upon practical surgery taught by experiments on animals. The importance of the chapter now and in the future hangs upon the fact that it is concerned with what every medical student should know. The question is whether a student can be taught and learn it all in any better way than the way in which Vesalius taught.

The following is a brief summary of the chapter.

The dissection of cadavers teaches the number, situation, shape, character and constitution of the several parts, whilst the vivisection of animals exhibits to the eye the functions of each part and supplies evidence on questions raised by the dissections. Hence the dissection of cadavers should come first, but be followed by vivisections.

The use of bones and cartilages in living animals is disclosed by producing fractures and dislocations, and by watching the union of fractures and the repair of joints.

The use of ligaments and tendons is studied by dividing them, *e. g.* the annular ligament controlling the tendons at the wrist, also the section of its different compartments on both the dorsal and palmar aspect, and the division of the several tendons of the flexor sublimis and of the flexor profundus digitorum.

The action of muscles can be directly inspected, the collecting and gathering together of the fleshy part when contracting, and again the thinning out in relaxing.

If in mice, " which," said he, "are numerous in our rooms," a cut is made longitudinally through the rectus abdominis, even throughout its whole length, the contraction of the muscle is not impaired, whereas even a superficial transverse cut across the muscle will abolish the contraction of the muscle.

Also, if the origin or insertion of a muscle is cut across, the muscle shortens in the reverse direction and loses its force. If both the origin and the insertion are divided, the muscle collects towards its middle but is powerless.

The nerves connected with muscles can be identified by ligaturing or by dividing them. The application of a ligature blocks a nerve, and on relaxing the ligature there is recovery. The nerves in the axilla or those going to the hind limb of a dog, or the median or ulnar nerves as distributed to the forearm and hand, may be exposed, although their distribution may not be exactly the same as in man.

The demonstration of the recurrent laryngeal nerves is done on a young pig (see the inset figure, *Fabrica* 1543, p. 661). The nerves are sought for and divided alongside the trachea, or they are simply compressed by a ligature, so that when relaxed the animal again cries.

By raising a nerve from its sheath, it can be seen that a nerve conducts through its substance and not through its sheath. This may be demonstrated by removing the sheath of the optic nerves, of the nerves of the arm or of the sciatic nerve.

The brain being exposed, the pulsation in the tortuous cerebral arteries become visible. Cuts can be made into the brain so as to penetrate to the ventricles, also segments of the brain may be removed. The brain may be injured by causing fracture of the skull and the results noted.

The function of the spinal cord can be exhibited by making various sections, following Galen.

The ribs may be exposed and removed without opening the parietal pleura, but so that the movements of the lung can be seen through it, or the pleura may be opened and the effect noted. The movement of the heart and lungs may be observed from below through an opening in the diaphragm, at the same time that the movements of the exposed diaphragm and intercostals are noted.

The heart may be exposed in a young pig

without opening the pleura, and the pulsation in the pulmonary artery or in the aorta checked by grasping it with the thumb and finger. The right and left ventricles may be cut into, also the auricular septum may be divided without arresting the movements of the auricles.

None of the coloured fluid given the animal to drink reaches the lung (a reference to a silly error in Hippocrates).

A ligature being rapidly applied around the base of the heart and the heart cut off, cats, and to a less degree dogs, could still make some movements of progression (*vidimus enim aliquoque etiam ita affecta canes, sed precipere feles cucurrisse*).

By repeatedly inflating the lungs, the movements of the heart may be kept up after laying open the thorax, and the simultaneous character of the systole with the pulsation in the thoracic and abdominal aorta observed as well as the pulsation in the tortuous coronary arteries.

" In order that the animal's life may be in some sort restored, an opening must be made in the stem of the trachea into which a quill or reed cannula may be inserted, connected with a pair of bellows; the cannula is then blown into in order to make the lung swell up. The animal thus takes in air to some extent, for with a gentle blast the lung will swell up as much as the cavity of the thorax allows. The heart then assumes again force and beautifully exhibits different movements.

"Therefore by once and again blowing up the lung, one can examine as much as one likes the movement of the heart, both by sight and touch. Also with the lung deflated one can grasp as well as view the trunk of the aorta both in the thoracic and lumbar region, and nothing is then clearer than the rhythm of the pulse of the heart and arteries, which having been observed sufficiently, the lung must be again inflated. And by this experiment—than which, to me, there is in anatomy none to be compared as more satisfactory—a good understanding of pulse differences may be got. When in turn the lung is let become flaccid, there is seen a wavy, wriggling and wormlike movement of the heart and arteries; and the lung being again blown up, the pulse becomes strong and quick and exhibits wonderful variations; and, as I said once before, this is the best sort of demonstration by which I am accustomed to exhibit the nature of all the pulses to a medical student."

The ligaturing of veins shows the various areas of blood supply and the sources of hæmorrhage from wounds. Experiments on arteries demonstrate the character of the blood in them, also that the pulse is derived from the heart and is transmitted through the column of blood and not through the arterial wall. When a cannula made out of a hollow reed is inserted into the course of an artery, such as the common femoral in the groin, and the controlling ligature between the heart and the cannula relaxed, the blood rushes through the cannula, and it can be seen that the artery pulsates below as well as above the cannula.

By other experiments the brain can be seen to be supplied not only through the carotid arteries, but also through the vertebral arteries, a fact overlooked by Galen.

The abdominal organs were made the subject of experiment: the suture of wounds of the intestines, the excision of the spleen, after which the animals lived. Vesalius excised the kidney in dogs, but, owing to difficulties in connection with the operation and the treatment of the wound, he failed to keep the animals alive. The results of castrating animals were observed, including those of excising from out of their capsules the substance of the testes and ovaries. Observations on the fœtus were made by using bitches and sows, in which the fœtus could be removed from its connection with the uterine wall, intact within its membranes. When laid on the table the fœtus within its pellucid membranes could be seen to make vain attempts to breathe and then to die of suffocation. If the membranes were laid open so that the head protruded it recovered and breathed regularly.

When, however, the uterus was simply laid open, the pulsation in the fœtal membranes and in the umbilical cord could be observed. In this state the fœtus made no attempts to breathe, not even when the membranes were laid open so as to expose the head, until the umbilical cord was compressed. Then it begun to breathe, although the pulsation in the uterine vessels could be seen to continue.

Discoveries in Italy by means of Experiments

Following Vesalius, and particularly in Italy, experiments on animals were pursued and discoveries in anatomy and physiology made.

Falloppio (1523–1562) corrected and added to Vesalius.

Eustachi (1524–1574) made famous engravings of dissections.

Aranzi (1530–1589) observed the fœtal circulation, the placenta and the image formed on the retina.

Fabrizi of Acquapendente (1537–1619) noted valves in the veins, the mechanism of respiration, the larynx as the organ of voice, the formation of the fœtus; Harvey attended his lectures.

Varolio (1543–1575) made discoveries on the brain.

Casserio (1561–1616) described the special sense organs.

Sarpi (1552–1623), the Venetian statesman, made experiments on the circulation and respiration.

Santorio (1561–1636) dealt with physiological statics and dynamics.

Aselli (1581–1626) discovered the lacteals.

Borelli (1608–1679), a mathematician, interested himself in the mechanical explanation of anatomical and physiological questions.

Redi (1626–1694), the learned physician in Florence, is famous for his observations on the genesis of insects, including flies, which he proved to arise always from ova, also for his experiments on the poisons of vipers.

Malpighi (1628–1694) described the microscopic structure of plants and animals, also the development of the embryo.

These discoveries had a direct bearing upon the future development of surgery; the most obvious were those described in 1680 by Zambeccari in a letter to Redi.

Joseph Zambeccari, a native of Florence, practised surgery and taught anatomy in Pisa.

Along with some colleagues he made various experiments on animals which he described in a letter to Redi in 1680.

He had excised the spleen in dogs, after ligaturing the splenic mesentery; none of the animals died and only two had a ventral hernia. In June 1680 he made his first experiment on excising the kidney, the ureter and the blood vessels being ligatured separately. The gall bladder was excised after ligaturing the cystic duct; in another experiment he simply ligatured the cystic duct. He thus disproved the assertion of Franciscus Sylvius that the bile was formed in the gall bladder and passed some up the hepatic ducts into the liver and the blood, and some down the common bile duct.

Zambeccari cut out from a kitten what he called the intestinum cæcum, by which he meant the appendix vermiformis, also he excised the intestina cæca from fowls. He ligatured and cut away a lobule of liver and the dog lived. An unsuccessful experiment was his attempt at excision of the pancreas.

The Spread of Medical Science from Italy to the North

Harvey (1578–1657), on his return from Italy, pursued experiments until he arrived at his demonstration that the blood circulates. To him succeeded the founders of the Royal Society, and their researches were published in the *Philosophical Transactions*, commencing in 1666.

The impetus derived from Italy gave rise in Holland to the founding of the University of Leyden, where Franciscus Sylvius (1614–1672), as Professor of Medicine, not only made numerous experiments himself relating to physiology, but encouraged others to do so, and also introduced from Italy the practice of Clinical Instruction by the bedside. His followers, Leeuwenhoek (1632–1723), Swammerdam (1637–1680), Graaf (1641–1673), besides others, each made discoveries of great importance. Boerhaave (1668–1738) was the chief teacher of medicine, and the development of surgery in the seventeenth and eighteenth centuries was greatly indebted to the Dutch surgeons. Von Haller (1708–1777) in his writings and by his experiments was the most important instructor of the Germans in the new physiology and surgery. Also from Leyden medical science was carried to Denmark by Thomas Bartholin (1616–1680) and by Steno or Stenson (1638–1686). Through Holland and Denmark may be traced the rise of medicine in Scotland by Alexander Monro I. (1697–1767), and to Scotland London was indebted for James Douglas (1675–1742) the anatomist and the Hunters.

Albrecht von Haller (1708–1777) by his experiments on animals contributed importantly to the progress of surgery in the eighteenth century. In the Preface to the sixth volume of his *Elementa Physiologiæ*, he gave a list of what he claimed as his own discoveries. In his *Opuscula Pathologiæ* he added sixty-three observations, as well as his experiments on respiration. In addition to teaching surgery at Göttingen, where he was appointed by George II., his *Bibliotheca Chirurgica* and his collection of Select Surgical Disputations are most valuable. The following is his declaration as to animal experiments:—

"A single experiment of this sort has often removed the errors arising from the work of entire years. This barbarity has been more useful to physiology than all the other arts, by the aid of which this science of ours has been established."

With this may be considered his extraordinary statement that he had never used a knife on a living man for fear of doing harm. His words were: "Although entrusted with a chair of surgery for seventeen years, and although I have frequently given surgical demonstrations, I have none the less never borne to cut a live man lest I should do too much harm. Verily, nevertheless, I have been present at many operations, have shared in consultations and have reported on questions under view, having followed surgical practice both in Paris and in the Charity Hospital." There follows a list of his surgical observations (*Bibliotheca Chirurgica,* II. 171).

THE ACADÉMIE DE CHIRURGIE

The advance of surgery in France during the eighteenth century becomes evident when one compares the writings of Paré, copied from Italian authors, with the papers on experiments on animals and surgery published in the memoirs of the Académie des Sciences and in those of the Académie de Chirurgie, and with the demonstrations given by Dionis (*d.* 1718) at the Jardin du Roi in 1707. Mareschall (1658–1736) and his pupil La Peyronie (1678–1747), in spite of opposition, succeeded in resuscitating the school of surgery of St. Côme, and they followed up this by founding the Académie de Chirurgie in 1732. In the memoirs of the Académie there continued up to the Revolution to be published papers on surgery in which the influence of experiments on animals is marked. In this they fulfilled the words of La Peyronie in the Preface:

"There are two sources whence flow the truths which can enrich our art, clinical observation and experimental physics. The plan which the Academy proposes to itself is to raise surgery on the basis of clinical observations, physical researches and experiments."

The progress made during this period in anatomy, physiology and surgery in France may be gathered from the works of Bichat (1771–1802).

THE "PHILOSOPHICAL TRANSACTIONS"

The *Philosophical Transactions* contain the description of a number of experiments having an important bearing upon the future of surgery, the chief of which may be noted down to the time of William Hunter. Besides the contributions relating to experiments, there were recorded a number of extraordinary cases in surgery. In addition there were included papers by Malpighi concerning experimental work done in Italy, by Leeuwenhoek in Holland, and others. Vol. I., 1666, comprises Lower's original experiment on transfusion in dogs, with further communications on the subject by the secretary Oldenburg and by Robert Boyle, as well as reviews of Redi's observations on the viper's poison, of Stensen's on muscles and glands, and of Graaf's collection and examination of the pancreatic juice. In the Vols. II., 1667, and III., 1668, besides communications on transfusion in man by Lower, King, Denis and others, there is included Hooke's experiment proving that the pulmonary circulation and the æration of the blood continued, although not only was the chest wall not moving, but neither were the lungs. Boyle, like Fabrizi of Acquapendente, injected medicated fluids into veins of animals. In Vol. V., 1670, Boyle described the effect on animals of exhaustion of air and of submersion under water. In Vol. XV., 1685, Howman of Norwich gave a very striking account of hydrophobia in a man, six weeks after being bitten by a fox. In Vol. XL., 1738, Nourse recorded a case of hydrophobia supervening nineteen months after being bitten. In Vol. XLIII., 1744, Ranby gave an account of a case of hydrophobia, doubtless hysterical, which recovered. In Vol. XLVI., 1750, Starr of Liskeard, supplied a most accurate description of rabies in a horse bitten on the shoulder by a mad dog. Vol. XXIII., 1703, contains Shipton's experiment on suture of divided intestine. In Vol. XXVII., 1712, among many experiments Courten included the results of administering to dogs, both by the mouth and by injecting into veins, poisonous doses of belladonna, colchicum and aconite.

In Vol. XXXV., 1728, Hall reported from Virginia several important experiments relating to the various circumstances under which a rattlesnake was made to bite a dog. I presume he was the first to make experiments in the United States. He managed to cause the rattlesnake to bite itself, and it died quickly from its own bite.

A decoction of laurel leaves was being largely used as a quack remedy, and several deaths had occurred. In Vol. XXXVII., 1731, Madden and Mortimer related a number of experiments on dogs which caused them to die from hydrocyanic acid poisoning, the conclusion arrived at being that a decoction of laurel leaves contained one of the most dangerous poisons hitherto known. In Vol. XXXIX., 1738, Belchier, surgeon to Guy's Hospital, stated that whilst dining on roast pork with a master dyer he had noted that the bones were reddened. The pigs had been fed on bran which had been boiled with calico sheets dyed with madder (*Rubia tinctoria*) in order to darken the colour. Further experiments were made by Duhamel de Monceau in Vol. XLI., 1744, and later by John Hunter, in connection with the development of bone. In Vol. XL., 1738, Fergusson in a letter to Cheselden said that as Cheselden had excised the spleen of a dog without harm, he would be interested to hear of a case of prolapse of the spleen, following a stab in the left hypochondrium. Fergusson tied a ligature tightly round the pedicle and cut away the spleen weighing 3½ oz. The man recovered.

In Vol. XLII., 1743, Tremblay described his experiments on water polyps which started the study of regeneration and reproduction. Vol. L., 1757, contains a notice of the colouring of the urine and milk red by the prickly pear of Carolina (*Opuntia*) and blue by indigo, when taken by the mouth; it anticipates a method for testing the activity of the kidneys. In Vol. LXIX., 1779, Fontana's experiments with hydrogen are given: this "inflammable air" caused the death of animals as quickly as did the carbonic acid or "fixed air" used by Boyle in his experiments.

The flourishing period of research by experiments on animals illustrated by the *Philosophical Transactions*, was enhanced by William Hunter (1718–1783), by John Hunter (1728–1793), by the pupils and assistants of W. Hunter, William Hewson (1739–1774), and William Cumberland Cruikshank (1745–1800); also by the successors of the Hunters, J. F. D. Jones, James Blundell (1790–1877), Herbert Mayo (1796–1852), and especially by Astley Cooper (1768–1841).

EXPERIMENTS ON ANIMALS BY THE HUNTERS, ASTLEY COOPER AND THEIR CONTEMPORARIES

William Hunter in 1758 demonstrated the absorbent functions of the lymphatics and lymphatic glands. Before that time attention had been chiefly paid to the lymphatic system in relation to physiology, and in anatomy to their junctions with the veins. Hewson distinguished the superficial from the deep lymphatics, and demonstrated that the lymphatic system is much more highly developed in man than in the lower animals, birds or fishes. Cruikshank, also with William Hunter, described the " Absorbing Vessels of the Human Body " in 1786.

In 1764, John Hunter bought ground out at Earl's Court where he constructed premises suitable for keeping the animals upon which he made his experiments. He ruptured his tendo Achillis in 1767, and that suggested experiments on the repair of the tendon, experiments supplemented many years later by Paget and Savory. These experiments have an important relation to the subject of the repair of tendons.

John Hunter's proposal for the " Recovery of People apparently Drowned," viz. the inflation of the lungs, involved a danger which he overlooked, because he did not keep alive the animals he used for his experiments. By keeping these animals alive, Leroy d'Étoilles and Magendie showed that inflation might rupture the lungs.

John Hunter in his treatise, *The Natural History of the Human Teeth*, published in 1778, included a chapter " Of Transplanting Teeth," in which he described the experiment of fixing the spur of a cock in its comb and the transplantation of its testes into its peritoneal cavity, experiments which founded the surgery of grafting skin and bone. Nearly allied were Hunter's observations on the growth of the antlers of deer in 1785, which suggested to him the idea of the collateral circulation by anastomising branches of arteries. It was in December of that year that he performed his first operation for the cure of aneurysm.

Hunter's experiments and observations on the growth of the bones, published after his death, directs attention away from the mechanical aspect to the active physiological processes, plainly indicated by the abundant and continuous circulation of blood through bone. There is still a danger of regarding the mechanical aspects of fracture and grafting of bone and of neglecting the physiological.

Hewson's experiments on the production of pneumothorax published in 1769, *i. e.* the effect of letting air into the pleural cavity of rabbits and dogs, are related to the treatment of tuberculosis by artificially producing a pneumothorax which is at present under trial.

Herbert Mayo proved by experiment that the facial and hypoglossal were pure motor-nerves, and thus put a stop to the erroneous practice of cutting these nerves with the object of relieving neuralgia.

Astley Cooper pursued surgical research by experiment on animals throughout his life. Perhaps the best-known experiments were those to be referred to later, viz. on ligature of the carotid, first mentioned in 1802, and those on ligature of the aorta, culminating in the operation on a patient in 1817.

It was noted that he was accustomed to take into his lectures small memorandum books; one remains preserved in the Library, which has, I believe, not been reviewed by any one. I have been allowed to copy it out and I hope to make it known. The book contains notes of experiments directed towards a number of moot surgical questions, made at his farm near Hemel Hempstead, beginning in 1826 and ending in 1830. I recall that in 1827 he was President of this College, and in 1828 was appointed Surgeon to the King. Some of the results of his experiments are preserved in the Museum, also in the Museums of Guy's and St. Thomas's Hospital. Perhaps the best evidence of Astley Cooper's knowledge and foresight are the regulations he made for the Triennial Prize which he founded at Guy's Hospital, and the six subjects he named, as the first to be set for his prize :—

(1) On the structure and use of the Thymus Gland.
(2) The structure and use of the Spleen.
(3) The structure and use of the Thyroid Gland.
(4) The structure and use of the Suprarenal Capsules.
(5) On the Blood and Blood Vessels in Inflammation as ascertained by experiment, injection and observations by the microscope.
(6) On the cause of the Coagulation of the Blood.

If one considers the state of medical knowledge in 1836 and the history of the subjects above named since that date, it can but enhance the reputation Astley Cooper gained in his lifetime, that at the end of it he should have made such a selection of subjects, first to be set for his prize.

J. F. D. Jones published in 1805 his important experiments on the control of hæmorrhage. Guided by experiment, Freer of Birmingham succeeded in ligaturing the external iliac artery for aneurysm after a much more prominent surgeon, Abernethy, who had not so prepared himself, had failed.

The experiments of Astley Cooper and Jones stimulated Scarpa (1752–1828) to a course of experiments on living dogs, sheep, oxen and horses, and upon the information so obtained he based his teaching and practice in the Hospital and University of Pavia. His writings obtained the widest circulation.

A miscellaneous series of experiments by James Blundell of Guy's Hospital exhibit the influence of Astley Cooper and are remarkable in anticipating advances, especially in abdominal surgery: Excision of a kidney and of the spleen; incision and suture of the urinary bladder; the effect of healthy urine let into the peritoneal cavity; excision of a Fallopian tube, of the ovaries and of the uterus; experiments relating to gestation in a Fallopian tube or cornu; experiments disproving the corpus luteum to be a criterion of past pregnancy; the production and suture of a vesico-vaginal fistula; the passage of coils of intestines through the fingers in the search for lesions, done repeatedly without causing death or extensive peritonitis; the ligature of abdominal arteries and the bringing out of the ends of the ligature through a separate button-hole; the suture of the abdominal wall; infusion of water to an amount corresponding to the blood lost.

Experiments relating to Surgery in the Nineteenth Century

In France, Bichat (1771–1802) in his writings, including with his *Anatomie Générale* the *Œuvres de Desault*, exhibited the intimate connection between surgery and experiments on animals. In particular his description of the naked eye anatomy and functions of the various structures is from that point of view of first importance to a surgeon.

Magendie (1783–1855) distinguished motor from sensory nerve roots. Flourens (1794–1867) discovered the functions of the semicircular canals and the cerebellum as regards equilibration. From Claude Bernard's (1813–1878) experiments, surgeons learnt about diabetes, vasomotor and sympathetic nerves, the function of the spinal accessory nerves, and how to make a gastric fistula. The experimental work carried on at Veterinary Institutions, such as Alfort, was of great value. Pasteur (1822–1895) starting as a chemist, began to work at crystallography in 1844, and he described the dimorphism of tartarate crystals in 1848. It led him on to the study of moulds and yeast and to the idea of alcoholic fermentation as the production of living organisms. This brought him into opposition with the highest authorities in science. In 1850 Claude Bernard declared that the process of fermentation was an obscure one, and in 1853 Dumas used the same expression. Berzelius held fermentation to be a catalytic process, and chemists, generally, at that time were united in rejecting living organisms as the cause of fermentation. After further observations on the production of lactic acid from milk, and of acetic acid from wine, Pasteur noted that a number of vibrios developed in albuminous media, with the production of foul gases. Thereupon, in conjunction with Claude Bernard, he commenced experiments on animals in April 1862.

Gradually chemists gave up the belief that fermentation was a catalytic process, and the ideas based upon that theory of fermentation which had been adopted to explain diseased processes had also to be rejected.

The positive proof that diseases were due to micro-organisms began to be established by the experiments on animals.

In Germany from about 1840 onwards a very great amount of research bearing on surgery by experiments on animals was carried out. The practical success which attended these researches and the influence the experiments have had upon the development of surgery was due to one circumstance in particular, the experiments were conducted by young surgeons already acquainted with surgery, under the supervision and help of the Professors of Physiology in the physiological laboratories of the Universities, and of the Professors of Surgery in charge of the surgical sections of the hospitals of the University towns.

In the United States surgeons carried out a successful series of experiments on animals, especially in connection with gastrointestinal surgery. The work had to be done in the face of popular ignorance and misapplied sentimentalism. The distinguished surgeon, Keen of Philadelphia, has fought the opposition continuously since 1884 and with success. Laboratories have been founded at the Universities and as part of special institutions, and remarkable advances in surgery have been made as the result of experiments, especially in relation to the surgery of the blood vessels.

In this country after Astley Cooper there was a very great neglect of experimentation. It is very much to be regretted that we should have fallen behind France and Germany. We may compare the mental attitude of John Hunter and Astley Cooper with that of

Erichsen, one of the best surgeons of his day. Both in his text-book (*The Science and Art of Surgery*, on the second page), and when at Philadelphia in 1874, he expressed himself in substance as follows: Surgery has attained its highest plane, and reached its limit of usefulness, and nothing in the way of improvement or advance need be looked for except in detail of technique.

It is a statement well remembered in America; indeed, I met with a recent repetition of it whilst preparing these lectures. Hence I have selected mention of it, from among other similar ones of that time. It was referred to as representing the idea of a London surgeon at that date. I may add that this opinion altered later, and he became greatly interested in the progress of experimental research. Revival in experimental research and a reformation in the attitude of the medical profession of this country towards experiments on animals was due, in London in particular, more than perhaps any one else, to Burdon-Sanderson (1828–1905), Professor of Physiology at University College, and later at Oxford. Moreover, the experiments of Ferrier on cerebral localisation, which he began at the West Riding of Yorkshire Asylum and continued with the aid of Gerald Yeo in London, were of first importance. They were carried out, in spite of much opposition. The direct result was the starting of the new surgery of the brain by MacEwen in Glasgow and Horsley in London.

EXPERIMENTS ON ANIMALS FOR THE PURPOSE OF ATTAINING MANUAL SKILL

A section of the Act 39 and 40 Victoria, c. 77, states, "The experiment shall not be performed for the purpose of attaining manual skill."

By this clause it is forbidden to gain skill, in a way which has been deemed of importance at every stage of the history of surgery. The spirit animating the clause stands in contradiction to common experience. I have given a summary of the teaching of Vesalius, and the final chapter of the *Fabrica* is the best classical exposition.

Horsley in his evidence before the Second Vivisection Commission in 1907, brought forward abundant evidence in opposition to the above clause. At the present time, perhaps, the merits of the question are better appreciated in the United States. At any rate, as far as I personally am concerned, the manual skill I gained whilst pursuing experiments on animals has been to me most valuable. The highest aim is that of discovery, exceptionally achieved; the general gain to the experimenter is that of skill and varied experience which can be applied to the practice of surgery.

I will confine myself to the mention of three surgical manipulations, for which the peculiar skill necessary must be acquired at the expense of human beings, unless by practising on animals before operating on patients.

(*a*) *Tracheotomy on a child suffering from diphtheria.*—For several reasons this urgent operation is nowadays rarely required of a surgeon. It is several years ago since I was called to operate on a baby, and I stated at the time that I had been able to perform the operation efficiently because in the course of a series of experiments I had often found it necessary to insert a tube into the trachea of monkeys, rabbits, cats and small dogs.

A house surgeon, who before he died attained to the first rank, was proved at the post-mortem on a child to have put the tube not into the trachea, but into the œsophagus, and to have scratched with his knife the front of the vertebræ.

(*b*) *The cure of hernia in a baby.*—This is a frequent operation, and, however often repeated, remains difficult to accomplish satisfactorily. I recall watching two surgeons operate for the first time for the cure of hernia. Both were well acquainted with the subject as then taught, and both had operated with skill on strangulated hernia. Both lost themselves at the operation and committed what are now called errors of technique, from which both patients died. I remain convinced that if before operating on patients they had each excised the patent funicular part of the processus vaginalis from some dogs, they would have succeeded at their first operation on a patient.

(*c*) *Operations on the interior of the eyeball.*—Operations on the eyeball form but a small part of the whole in modern ophthalmic practice. Opportunities for acquiring special skill by operating on patients come but seldom to the young ophthalmic surgeon. It may be years before he is able to get much personal practice, and then age may prevent him from attaining to the highest level of skill. It is therefore a question of acquiring skill when young by experimenting on the eyes of anæsthetised rabbits, or of gaining it slowly in the course of years and then perhaps only imperfectly, when operating on the eyes of patients.

II

EXPERIMENTS WHICH HAVE LED TO THE APPLICATION OF SURGERY TO THE ORGANS AND ORGANISED STRUCTURES OF THE DEEPER PARTS OF THE BODY

Transfusion of Blood and the Infusion of Fluids

Experiments on Transfusion of Blood and Infusion of Fluids, which occupied the attention of the founders of the Royal Society, were described in the first volumes of the *Philosophical Transactions*. They were the earliest experiments to be done in this country which particularly bear on surgery. By further experimentation during recent years methods have been so far perfected that many lives have been saved during the late war.

Experiments on Transfusion of Blood were begun in the hope that the blood, as the seat of life, might be restored when it has been lost. Besides this, it was hoped that old men might be rejuvenated by blood from a youth, and mental derangements relieved by the blood of a sane man. *Experiments on the Infusion* *of Fluids* were started owing to attention being drawn to poisons and poisoners.

The first to refer to direct arm-to-arm transfusion was Cardano in Italy, and an imaginary and ironical sketch of the procedure was given by Libavius in 1615; it may have been drawn from experiments on animals, but there is no evidence of the actual performance of the experiment.

"There is present a robust youth, healthy, full of blood, and a man exhausted, weak, lean, scarcely alive. The master of the art has two silver tubes, male and female, fitting into one another. He opens an artery [*sic*] of the sound man, inserts the male tube and blocks it. He next finds with difficulty the artery [*sic*] in the sick man and inserts the female tube. Then the two tubes arc applied together, when from the sound into the sick man there spouts hot and spirituous blood, bringing to him the spring of life and dispensing all languor."

Richard Lower on February 15th, 1665, in the presence of Robert Boyle and others, first bled a dog to syncope, and then transfused blood direct from the carotid artery of a second dog into the jugular vein of the first one. The experiment was very skilfully carried out, and it is now known that he escaped the drawbacks attending transfusion in man. The blood of one dog is compatible with that of other dogs; by first bleeding the receiving dog no plethora was set up; by skilful manipulation he inserted smooth silver cannulæ and connected the cannulæ so that there was no clotting; he was so clean that the operation did not excite septic complications. After repetitions on animals transfusion was tried on man and failed, for reasons discovered by further experiments in recent years.

Lower's experiment was repeated before the Royal Society at Gresham House. Pepys saw it carried out by Sir Edmund King and Thomas Cope on November 14th, 1666.

A spaniel was bled to syncope, then a little mastiff gave the blood, and died of the loss, whilst the spaniel receiving the blood, recovered, and was shown to the Royal Society a week later, November 21st, quite well. Lower and King on November 23rd, 1667, practised transfusion of sheep's blood upon a man in London, " in the presence of many considerable and intelligent persons." It was supposed that 9 to 10 ozs. had passed when the man said he thought he had had enough. But afterwards, for a consideration, he was ready for a second experiment, as he felt so much better.

Lower held that transfusion would be of service in anæmia. Denis repeated Lower's experiments in France, both on animals and human beings. Great harm was done by a recommendation of it for old age, lunacy and melancholia.

I saw once whilst a student transfusion attempted for the purpose of relieving pernicious anæmia. The two veins having been connected by an Aveling's ball syringe, at the second squeeze of the ball the recipient had a severe epileptiform seizure, which stopped the attempt.

After a renewed series of experiments transfusion in civil practice was revived in America shortly before the War. In this country there were also made important experiments concerning blood destruction, and Almroth Wright and others proved that coagulation could be held in check by fixing the calcium constituents of the blood by the addition of sodium citrate. In America in 1902 Carrel, and in 1907 Crile, by bringing endothelial surfaces into contact produced such smooth junctions between blood vessels that the blood passed the junctions without clotting. The lumen of connecting tubes were rendered smooth by sterile paraffin. In 1901 at the Institut Pasteur, Bordet and Gengou found that the blood of different species of animals presented differences in the ferment causing coagulation. The blood of one species promoted agglutination and dissolution of the red blood corpuscles of another species. Landsteiner, Moss and others applied this discovery to man, and found that the blood of human beings could be divided into four groups. It was thus rendered clear that one cause of failure had been the mixing of the two kinds of human blood, which were incompatible. Experiments on animals fixed the proper proportion of human blood and of sodium citrate solution, enough to check coagulation in the donor's blood without affecting the blood of the receiver.

Thus, during the late War, transfusion of blood could be carried out, either directly through tubes, which presented as smooth a lumen as a natural blood vessel, or indirectly, by hindering the coagulation of the blood as it was let from the vein into the solution of sodium citrate.

The *Experiments on the Infusion of Fluids* into the blood made at Oxford by Christopher Wren, Robert Boyle and Wilkins were described by Oldenburg, the secretary, in the first volume of the *Philosophical Transactions.* His article is entitled " An Account of the Rise and Attempts of a Way to Conveigh Liquors immediately into the Mass of Blood." An infusion of opium stupefied, without killing, the dog; an infusion containing sulphide of arsenic or antimony injected into the femoral vein of a dog caused vomiting and death; in other experiments spirits of wine and spirits of hartshorn were injected.

Also in the first volume of the *Philosophical Transactions* were described Redi's Observations and Experiments on the Poison of Vipers. A number of vipers had been collected for him by order of the Grand Duke of Tuscany in the hope that a theriac or antidote might be discovered.

Hall's "Experiments on the Rattlesnake in Virginia," published in 1728 in Vol. XXXV. of the *Philosophical Transactions*, were, I conclude, the first experiments ever carried out in the United States. He caused rattlesnakes to bite dogs; the experiments were most carefully made and recorded; he also managed to make a rattlesnake bite itself; the snake was nearly dead in eight minutes, and quite dead in twelve minutes. Pigs which forthwith ate up the snake suffered no harm.

A decoction of laurel leaves had become a popular quack remedy, and several mysterious deaths had followed among those who had taken the decoction. Madden of Dublin and Mortimer, the secretary of the Royal Society, described in 1731, in Vol. XXXVII. of the *Transactions*, experiments on dogs which proved that the decoction contained a very deadly poison. One hundred years later there were proposals, clearly made in ignorance, that hydrocyanic acid should be administered in order to avoid pain during a surgical operation.

In 1820 Magendie demonstrated that water might be injected into the veins of a dog after it had been bled, and in 1824 Blundell concluded from similar experiments that the infusion of water might be an efficient alternative to transfusion for puerperal hæmorrhage.

The obstacle in the way of advance was the ignorance as regards sepsis, and when, in 1855, Alexander Wood of Edinburgh advocated hypodermic medication in particular of morphia, there was danger until the means of preventing the introduction of septic infection by the syringe became known.

Cohnheim's experiments in 1869 showed the superiority over water of a solution of sodium chloride corresponding to the percentage of that salt in the blood; frog's muscle could be kept alive in it for two or three days. By very fine experiments Ringer proved that a frog's heart continued to beat longer if minute amounts of potassium and calcium chloride were added to the salt solution. Upon these foundations were based the experiments in 1879 of Kronecker and Sander, and of Jolyet and Laffonde. When a dog was bled from its carotid until half of the whole quantity of its blood had escaped, then, if nothing more were done, the animal died. If, however, immediately upon the bleeding, an equivalent quantity of normal salt solution was infused into the dog's vein, it lived and recovered from the loss of blood in the course of a few days.

From this date the intravenous infusion of the salt solution became part of general practice.

Later, as asepsis could be assured, salt solution was infused under the skin. The slow infusion by the rectum was begun by Murphy in Chicago (see Le Conte). A recent series of experiments by Bayliss led him to add gum arabic in order that the fluid should remain longer in the blood vessels, and this addition to the salt solution was widely adopted for the resuscitation of the wounded during the last year of the War.

Ligature of Blood Vessels

The application of the ligature for the arrest of hæmorrhage was practised by the ancients. Celsus mentioned the following ways of employing it. The ligature of the blood vessel on either side of the wound in the vessel, and its division between the ligatures; this was done in the operation for varicocele, also for the temporal artery after letting blood from that vessel. The ligature by transfixion was used for the removal of omentum prolapsed into the hernial sac. Piles were excised by cutting around and laying the ligature in the groove. Galen added the exposure and ligature of blood vessels around a tumour before commencing to cut it away. Paullos said that when an arrow-head was stuck in a blood vessel, a ligature must be applied to the blood vessel on each side, before attempting to extract the arrow.

This practice was lost under the Arabs, who limited surgery to what could be done by the aid of the cautery and caustics. In this they were followed by the mediæval surgeons. Paré had read the Italian surgeons, who had copied from the ancients without imitating them, and Paré is credited with the re-introduction of the ligature in a rough way, viz. by transfixing and ligaturing *en masse*, by which nerves and muscles were included in the knot. Neither Clowes nor Wiseman used the ligature when amputating. Both Sharp and John Hunter saw no harm in including nerves. When Lord Nelson's right elbow was shattered by gunshot at the attack on Santa Cruz, on July 24th, 1797, the surgeon on board the *Theseus*, when amputating, included the nerves in the ligature.

Nelson suffered great pain whilst at Bath; the ligature came away at the end of August, but it was not until the following December that the stump healed. This trying time and subsequent attacks of neuritis appear to have had a permanent influence upon his nervous system.

Experiments on ligature of arteries in continuity were revived by Lancisi in 1728, and he carefully separated the artery from its sheath and surrounding parts before applying the ligature. He then tied the iliac artery and Valsalva the carotid of dogs; the dogs survived until killed and examined.

Molinelli, MacGill and Guatani adopted this improvement when tying the brachial for aneurysm at the elbow. Molinelli had seen four cases of paralysis of the hand, because, in ligaturing the brachial artery, the median nerve had been included in the ligatures. M. Petit the surgeon, in 1731, as the result of a series of experiments, described what he called the "bouchon" or plug, *i. e.* the internal clot, and the "conuercle" or cap, *i. e.* the external clot. He thus gave an improved description of what happens when the cut end of an artery is tied.

Unfortunately, Dr. Petit, the physician, published in 1732 a paper advocating direct compression of a bleeding artery in lieu of the ligature. His erroneous notions were popular during the eighteenth century and were continually quoted, among others by John Bell in his *Principles of Surgery.*

Morand in 1736 advanced on M. Petit by describing the "froncement" or "crispation du tuyau," the crinkling or puckering of the cut end of the artery, by the contracting of the circular and longitudinal fibres, so as to reduce the orifice.

Between these experiments of M. Petit and Morand and those published in 1805 by J. F. D. Jones, various erroneous theories were promulgated to which Jones refers. The experiments made by Jones led him to distinguish the three coats of the artery, the cutting through of the inner and middle coat by the ligature, the elasticity of the artery by which when cut across its end retreats into its sheath. Besides the mechanical aspects, Jones dealt with the artery as a living structure supplied with blood vessels, lymphatic absorbents and nerves. As a result of injury by a cut or ligature, it inflamed, an exudation mingled with the internal and external clot; a contraction by scar tissue in and around the end of the artery finally incorporated it with the surrounding tissue.

The tight ligature which cut through the inner and middle coats was established by

Jones as the one method of application. This held good until Lister in 1869 soaked his ligature in carbolic acid. He ligatured the carotid of a horse by his antiseptic method and examined the condition of the ligatured artery five weeks later. Guided by this experiment Lister tied the external iliac artery for an aneurysm in the groin. The condition of the ligatured artery upon the death of the patient ten months later, from disease elsewhere, was described by him and corresponded with the results of the experiment on the carotid of the horse.

John Hunter had conceived the idea that a ligature might be applied to an artery in continuity, so as to compress it without injuring it. He and Cruikshank carried out a series of experiments, using strips of fine leather "French kid." The method failed, owing to sepsis.

In 1886, however, Ballance and Edmunds, experimenting under Lister's antiseptic precautions, and using the tendons of the tail of kangaroos, proved that large arteries could be securely ligatured in continuity without injuring the wall of the artery.

One proof of the importance of this form of ligature is that at last the abdominal aorta has been successfully tied. Keen in 1900 reported his as the twelfth case of ligature of the aorta.

All had terminated fatally, even the recent ones which had been done with precautions against sepsis. Keen's case died after forty-eight days, Tillaux's case after thirty-nine days, both from hæmorrhage at the site of the ligature.

In 1917 Hamann of Cleveland, Ohio, applied a ligature to the lower end of the abdominal aorta, which compressed the vessel. Pulsation in a vascular tumour was arrested and did not recur. The patient died six months after the operation, when the artery at the site of the ligature was found to have been compressed without being injured. A passage had been reformed through the constriction, $\frac{3}{16}$ inch in diameter, but the ligature had served its purpose.

THE ANASTOMOTIC CIRCULATION

Galen gave special attention to the anatomical anastomosis at the base of the brain, and the anastomosis of the arcades of the mesenteric arteries was also well known. But Vesalius and succeeding anatomists treated the arteria profunda femoris and the arteria profunda brachii as scarcely regular. In Cheselden's *Anatomy* as late as 1756 there is no recognition of the important part played by these deep arteries after the ligature of the brachial or superficial femoral artery. Surgeons began to operate for brachial and popliteal aneurysms with the haziest notions as to how the circulation in the limb beyond was carried on after the main artery had been tied. Many assumed that gangrene must follow, unless the aneurysm was placed on the radial artery below the bifurcation of the brachial, and that success occurred only when the commencement of the radial and not the end of the brachial was ligatured.

William and John Hunter began to study the subject by experiment. John Hunter in particular noted the anastomosis which restored the circulation supplying the deer's antlers. But it was Astley Cooper's experiments in ligaturing the carotids and the abdominal aorta and afterwards injecting the animal's vessels that the subject came to be generally understood.

Astley Cooper's experiments on the ligature of the carotid were described in his Lectures in 1802–1803. The injected specimen preserved in the Museum is from a dog in which within half an hour he tied both common carotids and both vertebrals. The dog became a good house-dog before being killed and injected. Branches of the subclavian arteries had anastomosed with the arteries of the head.

Astley Cooper found that a rabbit survived the ligature of both carotids, exceptionally also the ligature of the brachiocephalic trunk, but that ligation along with ligature of the left vertebral was always fatal.

The ligature of both carotids in the horse is invariably fatal. The vertebrals are very small and become mere threads before reaching the skull. The basilar artery is formed from the occipital branches of the external carotid.

In man an interval must occur between the ligature of the first and second artery for the development of a sufficient anastomotic circulation; the simultaneous ligature of the two carotids is fatal. Astley Cooper's first ligature of the common carotid on a patient was performed in 1805.

Stenson in 1664 had applied a ligature to the abdominal aorta of a rabbit which caused paralysis of the hind limbs, owing, as it was later demonstrated, to the thinness of the rabbit's abdominal wall, rendering the anastomosis inadequate. But when Astley Cooper experimented on a dog, the anastomotic circulation became established by intercostal and lumbar branches of the aorta above the ligature anastomosing with branches of the iliacs. The injected specimen is preserved in the Guy's Museum. Hence in 1817, when he found a patient suffering from a leaking iliac aneurysm, he tied the abdominal aorta as the only way of saving the man's life. The patient lived for forty hours.

SUTURE OF ARTERIES

Before the establishment of antiseptic methods, arterial suture was impossible owing to the secondary hæmorrhage which followed, and the suture of veins equally so, owing to the risk of a septic thrombosis.

A review of the earlier experiments illustrates the danger of arguing from analogy. In the case of the intestine success had been reached by turning inwards the cut edges of the mucous membrane, so this was adopted for the arteries also, with the result that the blood clotted on the rough margins and blocked the artery. The suture then had the disadvantages of a ligature in cutting off the flow of blood through the artery without the security afforded by the ligature.

In 1877, Eck (EKK) in St. Petersburg, with the object of finding a method for relieving cirrhosis of the liver and its complication, ascites, succeeded in making an anastomosis between the portal vein and the inferior vena cava. As it is impossible to arrest the circulation while the vessels are being united, Eck joined the two vessels by a ring of sutures corresponding to the outer ring of sutures employed in performing gastrojejunostomy. But before knotting the two ends of the suture upon the completion of the ring he passed blades of a pair of fine-pointed scissors, one into the lumen of each vessel. On closing the blades a longitudinal cut was made in the adjacent wall of the two vessels within the ring of suture. As the scissors were withdrawn, the sutured ends were tightened and knotted.

For physiological experiments, the Eck's fistula has been often repeated. The result is similar to the arteriovenous varix set up by the passage of a bullet. It has also been tried for the relief of ascites.

In 1902, Carrel instituted a fundamental improvement in the method of suture by turning outwards the rough edges of the artery wound and so bringing smooth endothelial surfaces into apposition. The inner aspect of the closed wound of the artery now presented no projection, and being quite smooth there was no occasion for the formation of any clot within the lumen of the artery. Moreover, healing was most active where the endothelial surfaces were in contact, just the reverse of that which happens in the intestines where there is no healing between applied mucous surfaces.

Carrel's experiments further demonstrated the necessity for absolute asepsis, as well as the advantage of using fine sewing needles threaded with silk lubricated by sterilised paraffin.

These experiments have guided surgeons in the suturing of wounds of arteries and in the cure of aneurysms when it has been advisable to avoid ligature of the artery supplying the aneurysm, lest gangrene of the limb should follow the cutting off of the blood supply. They have also been instrumental in improving the methods employed for the transfusion of blood. In the case of senile gangrene of the leg due to narrowing of the arteries, it has been proposed to restore the circulation of the foot by deviating the blood from the narrowed artery into the wider vein.

The experiments have been carried further and organs have been transplanted and the blood vessels of the transplanted organs connected up.

In 1912, Boothby described a series of experiments on cats under strict aseptic precautions, using No. 15 Kirby needles, and No. 200 cotton sutures, sterilised in white liquid petroleum. He succeeded in dividing the abdominal aorta and then reuniting it by suture; the lumen of the vessel was completely restored.

The Suture of Wounds of the Heart

Nothing is more striking than the immediate effect of a wound of the heart, and the various signs have been often described attended by a gush of blood, as in the death of the King of France, Henri IV. Sudden death following upon the withdrawal of the penetrating weapon occurred to Epaminondas at the battle of Mantinea. He had been transfixed by a spear, but could speak, and the surgeons feared to withdraw the spear. When he saw that his shield-bearer held his shield safe, and he was told that the Thebans had gained the victory, he ordered the spear to be withdrawn and forthwith bled to death, uttering the words, "Now is the time to die."

A similar sudden ending followed the withdrawal of the file with which the Austrian Empress was stabbed in Switzerland.

The special sign, that of the movement of the penetrating weapon by the beat of the heart, was noted by Homer, as already mentioned.

Celsus gave the signs of the more lingering death. "The heart being wounded, blood escapes in abundance, the pulse vanishes, there is extreme pallor. There occur cold and malodorous drops of sweat all over the body, the extremities become cold and death follows."

Until recent times attention was chiefly directed to the medico-legal aspects of wounds of the heart. Paré stated that a man, after being stabbed in the heart by a dagger, himself stabbed his adversary several times and pursued him two hundred paces before he fell dead. There was found to be a wound in his heart into which a finger could be inserted and much blood in the pericardium.

Schenck von Grafenberg noted that a student in Ingoldstadt, after being stabbed in the heart, ran the length of a long street and survived for an hour, quite clear in his mind. A wound traversing both ventricles was found.

A longer survival was described by van Heers. A man died seven days after his brother had shot him in the chest twice. The two bullets were found to have caused superficial wounds at the base of the heart without penetrating a cavity.

Scars in the heart wall in men whose history pointed to a previous injury of the heart were noted by Cabrol. Instances of injury to the hearts of animals and of finding bullets in their hearts are mentioned by Harvey and others.

Experiments on the hearts of animals had two preliminary difficulties to overcome. Galen exposed the heart without opening the pleural cavities in young pigs. In dogs this is impossible, for in them the heart is not in contact with the chest wall, and so a preliminary starting of artificial respiration is necessary before the heart is exposed. Also it is essential that the experiment should be carried out under strict asepsis.

Early experiments by Sanctorius and many others later were limited to puncturing the heart with a needle, when generally only a temporary disturbance was produced. The most important observation was that made by Morgagni, who noted that a mere puncture of one of the coronary arteries on the external surface of the heart might cause such an amount of hæmorrhage as to compress and arrest the heart. The grave and fatal importance of this collection of blood within the pericardium producing a compression of the heart was emphasised by him. It is now recognised as a principal reason for surgical treatment.

There is a very full account of Wounds of the Heart and Pericardium in the third edition of the *System of Surgery* by Holmes and Hulke, 1883, I. 843, by Alfred Poland and R. Lyell, based mainly on the 452 cases collected by Fisher in 1867.

The Suture of the Wounds of the Heart owes its beginning to the experiments on dogs by Del Vecchio. At the International Medical

Congress at Rome in 1894 he exhibited a dog on whom he had experimented forty days before. He had made two wounds in the heart, one of which had penetrated to the cavity of the ventricle. He had then sutured the wounds and the dog had completely recovered. Two days after being exhibited, *i. e.* on the forty-second day after the experimental suture, the animal was killed, and the wounds found healed. A scar on the endocardial aspect proved that the wound had penetrated to the ventricle. In the following year, 1895, Salmoni of Messina repeated these experiments, and exhibited two dogs, alive and recovered, fifteen and twenty days respectively, after the experiment. The dogs were killed and the wounds found soundly healed.

Thus encouraged and guided, Farina in Rome in March 1896 sutured a wound of the left ventricle and the patient did well until the fifth day, when he was attacked by bronchopneumonia and died on the eighth day. The sutured wound was healing by first intention.

In the same year Cappelen in Norway tied a large branch of the coronary artery which was bleeding, and the patient lived two and a half days. Also Rehn, in Frankfurt am Maine, exhibited a patient who had recovered after being stabbed a fortnight before. Rehn removed blood-clot from the pericardium and left pleura and sutured a wound of the muscular wall which had not penetrated to a cavity.

By 1912, 260 cases of such operations had been done, and recovery had followed in nearly one-half. There have been further lives saved during the War.

In 1907, Trendelenburg became impressed by the fact that some cases of pulmonary embolism did not die suddenly. He instituted a series of experiments in calves, the chief difficulty being that the pulmonary artery could not be clamped for longer than three-quarters of a minute. However, he learnt how to carry out the removal of the embolus, and in the following year opened the chest of a woman aged seventy within twenty-three minutes of the onset of the attack. Owing to age the patient did not survive. A second case done by Trendelenburg survived fifteen hours; a third case operated upon by Kruger lived for five and a quarter days.

In 1909, von Eiselsberg in Vienna opened the chest and sutured a punctured wound of the pulmonary artery. The man survived fifty-four days.

In 1902, Lauder Brunton raised the question whether it might not be possible to relieve mitral stenosis by mechanical means. In 1909 Bernheim succeeded in first producing a condition of mitral stenosis in dogs by means of sutures; later he relieved the artificially produced stenosis by establishing at a second operation a condition of mitral insufficiency.

RESUSCITATION FROM ASPHYXIA BY ARTIFICIAL RESPIRATION

The view of respiration handed down by tradition was that the "Breath of Life" entering from the outside air served for the refrigeration of the innate heat of the heart and for ventilation by which were expelled the fumes generated by such fire. This theory was only gradually disproved by a long series of experiments. The term asphyxia, or absence of pulse, is a misnomer. The ancient physicians were attracted by the loss of consciousness, which they assumed to be the result of cerebral congestion. Hence, treatment was directed to depleting the brain of blood containing the noxious fumes by means of venesection, when under low blood pressure intensely dark venous blood escaped slowly. With the same object in view, the interior of the nostrils was tickled by feathers, or irritated by drugs to promote sneezing and to excite nausea, in order to increase the downflow of pituita, the imaginary flow from the brain through the cribriform plate of the ethmoid. Pituita seems to have been a confounding together of the cerebrospinal fluid and of the nasal mucus.

The reference in the Book of Genesis to the "Breath of Life" implies that it was blown into the human body which had been formed out of the elements of the earth. Upon this conception was, no doubt, based the mouth-to-mouth inflation employed by Elijah and Elisha in order to revive the apparent dead. This practice has continued to the present for newborn infants.

In both ancient and mediæval times, when men were overcome by charcoal fumes, no direct measures were undertaken to restore respiration. The patients are generally described as cyanosed, but there are also references to a brick-red colour of the face, now associated with carbon monoxide poisoning. The phenomena following the pushing of a dog into the grotto near Naples was well known.

In A.D. 358, when the Emperor Julian was wintering in Paris, he was overcome by charcoal fumes. After being dragged out, the doctors made him vomit; he slept off the fumes and was all right the next day. His successor, Jovian, in A.D. 363, whilst on a journey to Constantinople was suffocated at night by the fumes of a charcoal brazier.

It is remarkable that there is no mention of the subject in the works of Oreibasios, Aetios, Alexander of Tralles or Paullos, and Cælius Aurelianus merely said that those who had lost sensation and movement from charcoal fumes did not usually recover.

Not much more was said on the subject of drowning. Opinion rested on the Hippocratic aphorism that "he who is being hung or submerged, is not dead whilst foaming at the mouth, but cannot be brought round." The application of warmth was based on the aphorism respecting treatment by contraries.

Galen's explanation was that, as under such conditions the breath of life could not escape by the throat, it was forced during the asphyxial struggles into the blood and humors, whence arose rupture of veins, hæmorrhages, effusions, apoplexy.

According to Galen, the danger of submersion was in accordance with the amount of water swallowed. Aetios said that a drowning man, after being pulled out, should be held head downwards and the epigastrium compressed to force out the water. The throat was to be tickled to promote vomiting, by which the pneuma or breath of life which had passed out into the body fluids might be expelled.

The modern idea on the matter was first expressed by Vesalius in 1543, as the result of experiment (p. 29).

The subject of respiration also attracted the attention of a group of men belonging to the Royal Society, and there are many observations included in the earlier volumes of the *Philosophical Transactions.*

Walter Charleton showed that in inspiration a vacuum is produced, and air enters whilst the lungs remain passive.

In 1660, Boyle demonstrated by the aid of the air-pump that in a partial vacuum a flame was soon extinguished, and a mouse and sparrow quickly died. This proved that air and not only the respiratory movements was essential, and that respiration resembled the burning of a candle. In 1670, he showed that animals living in water required air and did not breathe simply water. He placed living things, from small animals down to cheese mites, under the air-pump, and, the air being exhausted, the animals were convulsed and stopped breathing. Air being pumped in, after an interval, they recovered, animals and birds within two minutes, glowworms, tadpoles, leeches and insects survived and revived after longer periods, cheese mites survived in an exhausted atmosphere for three days.

Animals and land birds, when submersed, began to gasp after half a minute, and, if not drawn out at once, died. Ducks bore exhaustion of air under the pump no better than land birds; under water they did not gasp for four minutes. If not drawn out from under water within six minutes the duck could not be resuscitated. A bladder was oiled to make it translucent, a mouse put into the bladder: the neck of the bladder was then tied and the bladder put under the air-pump. As the air was pumped out, the bladder expanded. Boyle had thus produced the rarefied air, which causes mountain sickness. The mouse showed signs of distress and of nausea, but quickly recovered when the air entered the receiver again, and the bladder collapsed to its former size. When a frog was treated in this way bubbles of air escaped, just as from blood or milk. This was the first intimation of the production of divers' paralysis. In 1665, Hooke made his famous experiment. To the bellows used by Vesalius in the experiment described above, he attached a second bellows. By working the second bellows, the first was held constantly inflated and so the lungs. The dog was thus kept alive without any movement, neither of the chest wall nor of the lungs. Blood continued to circulate through the lungs. The dog lay still with the heart beating regularly, and with the conjunctival and iris reflexes active. It is an experiment which introduced the idea of apnœa, and has been revived of late years in connection with intratracheal anæsthesia.

In 1669, Lower in repeating Hooke's experiment noted that the blood in the pulmonary veins was red long before it reached the left auricle. He compared this with what was daily to be noted in the clot obtained by venesection. He thus concluded that the difference between arterial and venous blood lay in the air taken in and contained in arterial blood. Upon these discoveries Mayow, also in 1669, based his idea that air contained nitroærean particles which it gave up to the blood circulating through the lung, and which the blood in its turn gave up to the tissues. These nitroærean particles of Mayow were identified a hundred years later with oxygen by Priestly and Lavoisier.

The carbonic acid gas contained in venous blood had been referred to by the ancients under the term "fumus." Bacon called it "vapor carbonum," Van Helmont "gas Sylvestre," Black, in 1754, "fixed air."

Deaths by carbonic acid and carbon monoxide poisoning, also by drowning, continued to be noted without anything being done.

In 1651 occurred in Oxford the celebrated attempt to hang Ann Green for concealment of birth, and a biographical notice of this poor farm girl has been included in the *Dictionary* *of National Biography.* After her friends had pulled on her legs, Willis and Petty took her to their lodgings. Finding her still alive they did not apply any artificial respiration or inflation, only tickled her nostrils. After her recovery she was made to pay for the coffin which had been provided and to take it home, whilst the Oxford poets composed Latin verses on the occasion.

An early move in the direction of using means of resuscitation was started by John Fothergill; Tossach of Alloa in 1744 had described the case of a miner who, after being dragged out of a pit, lay for some three-quarters of an hour. Then Tossach applied mouth-to-mouth inflation and had the man "pushed and pulled and rubbed." Four hours later he was able to walk home.

Also Louis' experiments on resuscitating dogs after submersing them was instrumental in the founding of societies for the rescue of drowning people. A society was started in Amsterdam in 1767, in London in 1774. John Hunter's advice was asked; he does not seem to have made experiments actually pertinent to the question at issue, but advised inflation by doubly acting bellows. This inflation proved unsatisfactory, and its dangers were fully exposed in Magendie's report on the experiments made by Leroy d'Étoilles. The particular merit of their experiments was that the dogs had been kept alive after the experiments, and so it was proved that even moderate force in inflating the lungs tended to cause extravasation of air into the pleura and mediastinum owing to rupture of pulmonary vesicles. The outcome of Leroy's experiments was that intermittent compression of the chest wall was for the first time clearly recommended. The question was taken up by Marshall Hall, who in 1856 taught, as a result of his experiments, that the first movements in artificial respiration should be the compression of the chest, and then the natural resilience drew in air.

After an extended series of experiments Schafer's method became recognised as the best means of saving men from drowning.

Experiments by Claude Bernard explained the manner of carbon monoxide poisoning.

Hoppe Seyler in 1857 discovered that carbon monoxide formed a compound with hæmoglobin which required the presence of pure oxygen to dissociate it.

It is as the result of experiments, especially on dogs, that the knowledge concerning the gases in blood has been built up. Upon experiments on animals such as those conducted by J. Scott Haldane and others the methods now used for resuscitation in coal mines and other places have become established.

APNŒA

The state of apnœa was exemplified by Hooke's experiment above noted. An equally striking experiment was made by Mayow in 1668. After bleeding a dog he connected its vein with the carotid artery of a second dog. The recipient as it received the arterial blood, from breathing rapidly, scarcely seemed to breathe at all. The subject was neglected until interest was revived in it by Rosenthal. Its recognition is of great importance; a person may seem to be dead, his condition really resembling the state of an animal when hybernating.

B. W. Richardson in 1866 defined the limits of artificial respiration, that to be successful, the pulmonary circulation must be going on, the heart beating, however feebly. But Schiff in 1874 and many other physiologists found that by rhythmical compression the heart of an animal might be restarted. Arising out of these experiments, massage of the heart through the diaphragm after the surgeon's hand has been introduced into the abdomen, began to be practised.

By 1906, forty instances had been recorded, with nine recoveries and eight temporary survivals (*v.* Green).

Advances in pulmonary surgery have been

rendered possible by these experiments. In 1909, Meltzer and Auer made numerous experiments on dogs and established the method of intratracheal insufflation of the anæsthetic under a pressure of 15–20 m.m. Hg., the pressure being carefully regulated by a gauge; thus the objection shown by Magendie and Leroy d'Étoilles to forcible inflation was avoided. A catheter is passed so that air is inflated out of its end at the bifurcation of the trachea; the used air containing carbonic acid gas returns beside the catheter through the larynx outwards.

One set of their experiments I do not think has yet been applied to man. They gave dogs double the poisonous doses of strychnine and then kept up intratracheal insufflation until, after seven to eight hours, all the strychnine had been eliminated by the kidneys. This was done without the slightest injury to the trachea or lungs of the dogs; as the respiratory spasms passed off, the dogs started to breathe spontaneously and recovered.

The success of the application of surgery to the injuries of the chest in the late War is well known. Willy Meyer of New York in a series of experiments on dogs excised part of the lung, with recovery in five out of six. It has pointed a way to the relief of that exhausting condition bronchiectasis, and the patient may be relieved from continually coughing up foul pus if the affection is restricted to one lobe of a lung.

INTESTINAL SUTURE AND ANASTOMOSIS

The ancients applied sutures to wounded intestines when prolapsed, but the exact procedure is not described. Susruta and the Arabs mention the use of antheads for the purpose, reported in recent times as still practised in Dalmatia, Algeria and Asia Minor. The effect would be similar to the application of a Michel's clip, the edges would be turned in and the peritoneal surfaces brought into apposition, as with Lembert's sutures. The procedure described by Roland and the Four Masters, hence often called by the name of the latter, involved the use of a tube of elder or the trachea of an animal, and the wound was closed over the cylinder. Cheselden mentioned that a veterinary surgeon had employed a keck, that is, a piece of the hollow stalk of hemlock. He had cut off 3–4 inches of the gangrenous intestines which had prolapsed through a wound an ox had received, and joined the ends over the tube. An hour after the closure the ox dunged and lived to work for several years after.

An experiment was made by Shipton in 1703, recorded in the *Philosophical Transactions;* he cut out two fingers' breadth from the ileum of a dog and united it. When the animal was killed three weeks later the gut was found united except that the margin had separated a little, but the junction had been covered by omentum and adhesions.

The experiments and observations made by Bichat distinguished for the first time the part played by the peritoneal surface of the intestine, and that of the mucous membrane. Adhesions took place between the serous, peritoneal surfaces like those which occurred between the margins of wounds of the face which heal by first intention. The mucous surfaces did not form adhesions, and the secretion of the mucous surface was an obstacle to healing.

Unfortunately, Travers in London was ignorant of or ignored the description given by Bichat, and in 1812, after making some rough experiments, such as stabbing the abdomen of horses with swords, he concluded that intestinal wounds could not and did not unite, but were closed by surrounding peritoneal adhesions. The writer of the article in Holmes' and Hulke's *System of Surgery,* 1883, seems to have ignored the French experiments, and to have blindly followed the errors made by Travers.

In 1824, Jobert in Paris recalled Bichat's distinction between the peritoneal surface which exuded a membrane such as united a wound of the face, and the mucous surface with its secretion from its follicles. Based on this, Jobert experimented by turning in the margins; then the needle and thread was passed through the inverted edges, *i. e.* the needle penetrated the intestinal wall four times. The objection to this suture was that it set up a valve-like obstruction which narrowed the lumen of the gut, owing to the turning in of the edges.

It was in order to do away with this valve-like obstruction that Lembert in 1827 invented the suture known by his name. He described it as the suture one would naturally apply to a wound of the intestine which had penetrated the peritoneal and muscular coat, but not the mucous coat. Jobert repeated Lembert's experiments, and objected that Lembert's suture was too weak when the whole wall of the gut was cut through. Therefore in his second communication he described a modification of his first proposal, which is practically identical with that revived by Czerny in 1878.

Gély of Nantes, in 1842, was the first to conceive the idea of a lateral anastomosis. The union of the two coils of intestine had been observed to result from bullet wounds, and Gély attempted to imitate this by making a wound in two adjacent coils, then applying one wound against the other. He used the term " Adossement," or back to back.

Maissoneuve, in 1844, improved on Gély's experiments and adopted the name " Anastomose intestinale " or " Enterostomie." The object of his experiment was to avoid the necessity for the making by the surgeon of an artificial anus.

Between September 11th to October 25th, 1844, Maissoneuve made eight experiments on dogs; six recovered with the lateral anastomosis and had free motions. Then in a patient suffering from intestinal obstruction, he made a lateral anastomosis between the ileum above and the colon below the obstruction. Fæces passed, but owing to a leakage between the sutures fatal peritonitis followed. In a second case of the relief of intestinal obstruction, the patient died in forty-eight hours. The Société de Chirurgie, led by Dupuytren and Chassiagnac, opposed Maissoneuve's anastomosis and still favoured an artificial anus, their main objection was that a fæcal accumulation would occur in the excluded portion which would destroy life.

As a result the lead passed from France, and the succeeding experiments were done in Russia and Germany. In 1861 Haken carried out numerous experiments at Dorpat, in 1875, Ischetnevsky-Bourchensky cut out a piece of intestine in thirty-five dogs with twenty-nine recoveries. Guided by such experiments, Pirogoff, when he was confronted with a coil of intestine, perforated by four bullet holes, excised four inches of bowel and joined the ends. Recovery followed.

In Germany the experiments originally devised in France were repeated by Emmert of Giesen in 1862, by Wysler of Aarau in 1865, and by Czerny in 1878. Then Koeberle of Strasburg reported that he had cut away two yards of gangrenous bowel, and Arnaud removed seven feet; both patients survived.

Next followed the great advance made by Mikulicz. On October 7th, 1880, he closed an ulcer of the stomach which had perforated. The perforation was near the cardiac orifice, and he used nine Lembert's sutures. The patient died three hours later, but the post-mortem proved that the operation had been satisfactorily performed and the ulcer closed. Mikulicz gained his first success in 1884; the perforation was closed and the patient recovered.

In America the fatal results of gunshot wounds of the abdomen gave rise to experiments by S. D. Gross and others, and in 1882 Marion Sims appealed to surgeons to adopt an operative in place of an expectant treatment.

In 1884, Charles T. Parkes of Chicago experimented by firing pistol bullets into the abdomen of dogs. The results illustrated the danger arising from extravasation of fæcal contents and of mesenteric hæmorrhage. In forty-five dogs he united the wounds by Lembert's sutures, or when the wounds were close together he excised the damaged segment of gut. Parkes' experiments guided Bull of New York when he operated upon a man who had been shot in the abdomen by a pistol. He removed the bullet and sutured the wound in the intestine. The patient made a complete recovery.

Subsequently hundreds of cases were so treated in the United States. In a case successfully operated upon by Woolsey there were sixteen perforations, in one by Matas of New Orleans twenty perforations.

Some experiments by Halsted in 1887 disclosed an important matter, not well recognised before. The submucous layer had been ignored; Halsted demonstrated it by scraping off the other layers. There remained a tough membrane, the basis of catgut and the main component of sausage skins. Sutures hold longest in the submucous layers.

During this period, from Lembert onwards, practically no part was taken by English surgeons. The only instance, I believe, worthy of mention were the experiments done by Stanmore Bishop at Owen's College, Manchester. He made some careful experiments, and his animals were particularly well looked after. The method of suturing he described is essentially the same as that commonly used at present when performing gastrojejunostomy. Specimens from his experiments are preserved in the College Museum.

The Operative Treatment for Intestinal Obstruction continued to be influenced by the rejection in France of Maissoneuve's proposals. I recall that at the Bath Meeting of the British Medical Association in 1878, Jonathan Hutchinson said that in cases of uncertain diagnosis it was better to trust to the chances of spontaneous cures or to try to obtain relief by abdominal taxis, inversion and copious enemata, rather than to resort to exploratory operations.

In desperate cases he advocated Nelaton's operation, that of opening the first distended coil met with. Whilst acting as house surgeon, I assisted a surgeon to do this; there was a gush of fæces, at which the surgeon expressed satisfaction; but the flow quickly ceased. At the post-mortem examination it was found that the dilated apex of a volvulus had been opened, and the operation had so fixed the gut as to prevent all possibility of recovery.

In 1888, Senn of Chicago described a number of experiments he had made on cats and dogs, in order to find out how the various forms of intestinal obstruction might be dealt with. He then went on to apply his experience to human beings. His experiences constituted the beginnings of the application of surgery to these difficult and fatal conditions. As aid in these operations, Senn for a time used his "bone-plates."

Subsequently Murphy, also at Chicago, made a large number of experiments on dogs and invented his "button." This proved a better aid than the "bone-plates" and constituted a greater encouragement to surgeons to undertake these operations.

After practice surgeons have found themselves able to dispense with these aids, but the experiments both of Senn and Murphy, taken in connection with their operations for intestinal obstruction, make up a chapter of surgery which should be well known.

GASTROSTOMY

Gastric fistulæ, whether the result of accident or disease, had been often noted. Attention was especially attracted to the case of the Canadian half-breed, Alexis St. Martin, which was so thoroughly investigated by William Beaumont of Connecticut, a surgeon in the United States Army. It was suggested by Egbert of Christiania in 1837 that an artificial fistula should be made to prevent death from starvation in patients suffering from stricture of the œsophagus, the operation being done in two stages.

In 1842 Bassow, and in 1843 Blondlot, succeeded in establishing an artificial gastric fistula in a dog. Blondlot drew out and fixed a cone of the stomach in the abdominal wall, the cone being held in place by a pin. The apex of the cone was then constricted by a wire under the pin until in a day or two the tip of the cone sloughed off. In 1843, Claude Bernard made use of two flanged tubes, practically an early form of Murphy's button. The methods were improved in physiological laboratories; Lauder Brunton in the *Handbook for the Physiological Laboratory*, in 1873, described that of inserting and fixing a catheter, which was retained. Unfortunately, surgeons, whilst attempting gastrostomy, failed to practise it first on animals, or indeed to acquaint themselves with the method approved in the physiological laboratory. Operations on man were commenced by Sédillot of Strasburg in 1849. Subsequently some forty-five attempts were recorded, all failures, until Sydney Jones at St. Thomas's Hospital in 1875 experienced a recovery in his third case. His patient had malignant stricture and died forty days later. In 1876, Verneuil succeeded in giving permanent relief in a case of simple œsophageal stricture. But even in 1894, the immediate mortality of gastrostomy for œsophageal stricture was found to vary from 30 per cent. in inflammatory cases, to 80 per cent. in malignant ones.

Then Stamm of Cleveland, Ohio, repeated the experiments on the lines described in the *Handbook for the Physiological Laboratory* twenty-one years before. He fixed in a No. 15 English catheter; in the same year Emmanuel Senn described on dogs the inversion to form a valve, and Kader in Germany and Bidwell in London carried out the operation as now generally done.

I am glad to point out the best and earliest description of how to perform gastrostomy in the much-abused *Handbook for the Physiological Laboratory*, the articles being written by Lauder Brunton, a physician devoted to experimental research.

GASTROENTEROSTOMY

Maissoneuve's method of lateral anastomosis was applied to the surgery of the stomach in 1881 by Wölfler in Vienna. On September 28th, 1881, a man was found to have an irremovable cancer of the stomach, and Nicaladoni, who was assisting the surgeon Wölfler, is said to have suggested the operation. The anastomosis was made between a coil of jejunum 50 cm. from its commencement and the anterior wall of the stomach, 5 cm. above the greater curvature. The suture used was that of Lembert, following Maissoneuve's experiments; the man was temporarily relieved, and when he died a communication 2 cm. in diameter was found. Billroth operated on a similar case four days later, but he made a spur and the patient died of biliary vomiting, since known as the circulus vitiosus.

The further improvements in gastrojejunostomy were aided by additional experiments on dogs. In 1882 Lücke used clamps; in 1883 Courvoisier joined the jejunum to the posterior wall of the stomach, a method further improved by von Hacker in 1885. The scope of the operation was widened by Fritsch in 1887, who adopted the operation for the first time for the relief of simple gastric ulcers. Some surgeons, when they began to practise the operation, aided themselves by using Senn's bone-plates or Murphy's button. The present-day operation came into vogue after Petersen's report on Czerny's cases on Heidelberg to the Paris International Medical Congress in 1900.

GASTRECTOMY

In 1780, Merrem cut out the pylorus of dogs and joined the stomach to the duodenum. One dog recovered out of the three. Nothing more was done until Billroth and his assistants, Gussenbauer and von Winiwarter, in 1876, resumed the experiments and used the sutures originally described by Lembert and Jobert. In 1878, Kaiser succeeded in removing all the stomach from a dog, and the animal during the following eight months increased in weight by nearly a half.

Guided by these experiments, Billroth successfully removed a cancer of the stomach on January 29th, 1881. The two methods he devised are commonly known as Billroth I. and Billroth II. (*v.* Wölfler).

CÆSAREAN SECTION

Lembert's method of inserting sutures, when applied to the closure of the wound in the uterus, made that most ancient operation, Cæsarean section, safe. Previously the wound was generally left unsutured, the few cases which survived, *e.g.* Edmund's cases, did so because the contraction of the uterus happened to close the wound so that the lochia did not escape into the peritoneum. If sutures were so applied as to penetrate to the uterine cavity, septic inflammation and death always follows.

Keyser and Sanger in 1882 succeeded, partly because they adopted Lister's antiseptic method, and partly because they inserted sutures after Lembert's method which prevented the lochia from leaking into the peritoneal cavity but did not penetrate to the uterine cavity.

Indeed, Cæsarean section can be done more than once on the same woman for the operation leaves hardly any scar.

Suture of the Abdominal Wall

Celsus and Galen described at length the various ways of closing a wound in the abdominal wall, which were copied by surgeons down to Spencer Wells. Ventral hernia frequently followed the operation of ovariotomy, and at the post-mortem examination of his fourth case Wells recognised that the procedure he had used was bad. There was, in particular, doubt whether the peritoneum should be included in the sutures, so at the request of Wells, Benjamin Richardson experimented on eighteen animals. After cutting through the abdominal wall, in imitation of the incision in ovariotomy, sutures were inserted, some including the peritoneum, some not. As the wounds in which the peritoneum was included healed much more firmly, Wells adopted the method. Billroth, as the result of experiments, commenced the method of suturing in stages in 1881.

BILIARY SURGERY

According to the aphorisms of Hippocrates, injuries to the liver, from which the gall bladder was not distinguished, were absolutely fatal; the wounds made by the surgeon's knife were classed as injuries. Moreover, the humoral pathology so obsessed the minds of physicians, that no ancient writer made mention of gall stones until the fourteenth century, although they have been found in Egyptian mummies. From, however, mediæval times onward gall stones and the obstruction caused by them were frequently noted. In the eighteenth century, van Swieten in his *Commentaries on Boerhaave's Aphorisms* has a section entitled " Of an Hepatitis and Jaundice," in which he gives a clear account of jaundice due to obstruction by gall stones. Yet if one turns to Quain's *Dictionary of Medicine*, published in 1883, and reads the articles by Murchison and by Wickham Legge, one finds no reference to the surgical treatment. The general treatment was still that of depletion by purging; venesection and emesis had already been given up. Ox bile might be administered by the mouth to replace the deficiency of bile in the duodenum, and as turpentine dissolved gall stones in a test tube, it might be given by the mouth with that object. It was also injected into the biliary fistulæ which were of common occurrence.

In 1680, Zambeccari cut into the gall bladder of a dog, then sutured the incision, and the dog recovered. By this experiment he disproved the assertion made in the Hippocratic aphorism. In another dog he separated the gall bladder from the liver up to the cystic duct to which he applied a ligature, and cut the gall bladder away beyond the ligature. The dog recovered, and on being killed and examined two and a half months later, the site of the gall bladder was found to be occupied by omentum adherent to the liver. The common bile duct was continuous with the hepatic ducts in the liver without any hindrance. This experiment proved that no harm followed the removal of the gall bladder, at the same time that it disproved the opinion of Franciscus Sylvius at Leyden, that the bile was formed in the gall bladder.

Zambeccari's experiments were repeated and confirmed in 1767 by Herlin, who suggested that for the removal of gall stones the operation should be done in two stages. The first stage should consist in fixing the gall bladder to the abdominal wall so that it might become adherent.

This recommendation was ignored by those surgeons who cut into the gall bladder, hence the patients died of peritonitis. In the first case which survived, done by Bobbs of Indianopolis on June 15th, 1867, recovery was due to the gall bladder having become spontaneously adherent to the abdominal wall. After the removal of the gall stones the wound was sewn up and the patient was alive in 1899, thirty-two years after the operation, but in some trouble apparently from another gall stone.

The gall bladder was first excised from a patient by Langenbuch, in the same way as Zambeccari had done it on dogs nearly two hundred years before. Subsequently Langenbuch reported that he had performed the operation in twelve cases without a death.

In order to overcome a permanent obstruction to the common bile duct, Gaston of Atlanta, Georgia, experimented by uniting the gall bladder to the duodenum in dogs. Further experiments were made by Dastre in 1889. The operation on patients was found difficult; of twenty-three cases so operated on, eight died from the operation. But Murphy, after experiments with his button, operated on seventeen patients between July 11th, 1892, and December 1st, 1893, and all recovered.

Later, with practice, surgeons have been able to operate successfully, using sutures only.

THE SURGERY OF THE SPLEEN

The spleen is the one abdominal organ which the ancients found could be cut out and the animal survive. In 1680, Zambeccari and his friends excised the spleen from dogs and subsequently examined the animals. All that was found were adhesions, and in one instance a nodule containing pus where the ligature had been applied. In 1735, John Fergusson, in a letter to Cheselden, wrote: "You have taken out the spleen of a dog without any remarkable inconvenience, yet it has never been attempted, that I know of, in a human body." He then went on to tell how, emboldened by Cheselden's experiment, he had himself removed the spleen from a man. On January 5th, 1734–5, a man was wounded by a skean, or great knife, which passed through the muscular part of his left forearm and penetrated his left hypochondrium. Twelve hours later Fergusson found the man's spleen, cold and black, projecting through the wound, and so swollen as to be irreducible. He therefore applied a ligature and cut the spleen away. The man recovered. A prolapsed spleen was removed by Vater after the battle of Dettingen; also O'Brien did the same in 1818. Astley Cooper seems to have been the first to observe a case of torsion of a movable spleen. "A lady under the care of Drs. Babbington and Lettsom, after vomiting severely and repeatedly for a week, died. A swelling in the lower part of the abdomen was found after death to be an enlarged spleen turned half round upon the axis of its blood vessels so that the return of blood by the splenic vein had been interrupted, although the splenic artery was not obstructed." Attempts to remove the spleen from within the abdominal cavity in the first half of the nineteenth century failed through sepsis. In 1865, Spencer Wells cut out an enlarged spleen from a woman, but the patient died six days later from thrombosis and sepsis. Improvement followed upon the adoption of Lister's antiseptic precautions. In 1867, Péan successfully removed an enlarged and cystic spleen; Spencer Wells performed his second splenectomy in 1868, his third in 1876 and his fourth in 1887.

A series of experiments made by Mosler on dogs and rabbits in 1872 has proved to be important to surgeons as indicating what is likely to be the course after operation. The removal of the spleen caused a temporary disturbance, a rise of temperature, loss of weight, general enlargement of lymphatic glands, an increase of red marrow in the bones, a diminution of the red corpuscles in the blood and an increase of white corpuscles. These manifestations passed off as the work of the spleen was taken over by other organs. In some instances there was hypertrophy of accessory spleens, splenculi.

The operation for the removal of a ruptured spleen, hitherto a fatal accident, was first successfully accomplished in 1893 by Riegner of Breslau. This was followed by three cases in 1896 by Bernard Pitts and Ballance at St. Thomas's Hospital. The disturbance which followed was similar to that described by Mosler from his experiments, and proved temporary, the patients making a good recovery.

The Surgery of the Pancreas

The pancreas was included by the ancients among the lymphatic glands in that region, and derives its name from the idea that it was composed of undifferentiated flesh which filled up the spaces between the blood-vessels. Galen said that Herophilos and Endemos, and they alone, had stated that there poured out from the pancreas a fluid into the intestines. Galen did not accept this opinion, and it was not until 1642 that the pancreatic ducts, both the main and the smaller duct, were described by Wirsung, a Bavarian, then Professor of Anatomy at Padua. Wharton in 1656 attributed to disease of the pancreas certain signs. The next step forwards was made by Regner de Graaf in 1664 at Leyden. He took a long thin quill from a wild duck, passed it into the pancreatic duct of a dog and collected the pancreatic juice. The experiment is described in Volume I. of the *Philosophical Transactions*. From a large dog he collected one ounce. Whilst de Graaf and his teacher, Franciscus Sylvius, attached special importance to the pancreas in digestion, opinion in general treated the influence of the pancreas as of small moment until after Claude Bernard's experiments.

Claude Bernard proposed to himself to track out by experiments on animals the starch and sugar taken in as food. By following up this course he found that in over-fed dogs the liver stored up a special substance, glycogen. He began publication of his researches in 1849, and later his attention was turned to the pancreas. In a proportion of cases examined after death from diabetes, fibrosis of the pancreas and pancreatic calculi are found. In 1889, Miakowski and V. Mering took advantage of the anatomical relations of the pancreas of the dog. In that animal it is a floating organ, placed between the layers of the mesentery; hence the pancreas can be excised from the dog, a measure impossible in other animals. After removal of all the pancreas from a dog, a large amount of sugar appears in the urine. But the pancreas is a complex organ, and Senn in 1884, by his experiments on the removal of the pancreas from dogs, showed that extravasations of the pancreatic juice tended to set up fat necrosis and gangrene.

Opie's experiments were particularly important as explaining the way in which hæmorrhagic pancreatitis arises, also interstitial pancreatitis, and pancreatic cysts. Opie injected bile into the pancreatic duct of a dog, and so produced hæmorrhage into the substance of the pancreas, also around the pancreas and in the adjacent mesentery and omentum. The bile set up necrosis and upon the necrosis followed hæmorrhage, although micro-organisms were absent.

The present position of pancreatic surgery has been arrived at under guidance of the foregoing experiments.

III

IMPROVEMENTS IN SURGERY

Discoveries made by experiments on animals have enabled the scope of parts of surgery to be extended indefinitely. On the other hand, some discoveries have resulted in improvements in medical treatment, and have rendered unnecessary indifferent surgical treatment previously practised.

The Nervous System

The experiments on the nervous system which resulted in such great advances in surgery, as contrasted with experiments on other subjects previously noted, were mainly carried out in this country.

Experiments on such a complex organ as the brain, together with pathological observations, demand interpretation, if any useful purpose is to be served.

A general theory of the nervous action, the most remarkable since Galen, was published in 1784 by Prochaska (1749–1820), Professor of Anatomy and Physiology in Prague.

Prochaska made the following divisions: (1) the organs of the mind associated with the faculty of thinking; (2) the sensorium commune, which, from above downwards, included the brain matter composing the roots of the cranial nerves, the medulla oblongata and the spinal cord; (3) the nerves viewed as prolongations from the sensorium commune.

There was a force innate in nervous matter to evoke which a stimulus was required: (*a*) any stimulus or irritation applied to the exterior or interior of the body; (*b*) a stimulus arising only in the mind.

The sensorium commune reflected sensorial into motor impressions: (*a*) in the absence of consciousness, in sleep, in animals after decapitation, in patients suffering from apoplexy, and in epileptic fits. The reflection might occur through segments of the brain, of the spinal cord, or through ganglia unconnected with the spinal cord or brain.

(*b*) Connected with consciousness, the mind might simply direct or moderate reflex acts, also it produced them as psychical or mental acts by the force innate in nervous matter.

It was especially the general view of Hughlings Jackson eighty years after Prochaska, which he formed of the nervous system, his remarks on "Evolution," and "Dissolution" on "Destructive and Discharging Lesions" which suggested experiments and constituted the best guide in the interpretation of results.

SURGERY OF NERVES

In the eighteenth century there was still a great lack of knowledge concerning both cranial and spinal nerves. The hypoglossal nerve was considered a nerve of taste, and the fifth nerve the motor nerve of the face. As the facial nerve was supposed to be a sensory nerve, it was held to be the seat of neuralgia and so it was divided. Herbert Mayo in particular, in 1822, by dividing the hypoglossal nerve on one and then on both sides in an animal, proved that it was purely a motor nerve, sensation being retained after its division. Also he demonstrated by other experiments that the facial nerve was the motor nerve of the face, and the small root of the fifth the motor nerve to the muscles of the lower jaw.

Old time surgeons were afraid to suture wounded and divided nerves for fear of setting up tetanus. The practice of applying sutures only became general with the antiseptic era.

There has been, and still exists, a great diversity of opinion as to regeneration of nerves. After Waller, in 1851, had described how the portion of the nerve cut off from its ganglion cell degenerates, improved histological staining methods arising out of the experimental work and the staining methods of Marchi and of Golgi, permitted of degenerating fibres being distinguished in the nerves and central nervous system. Embryological researches demonstrated that nerves were produced as outgrowths from the ganglion cells. Hence it came to be generally accepted that after division, nerves regenerated by outgrowths from the proximal end.

On the other hand, Bowlby demonstrated as early as 1884 what appeared to be regenerating fibres in the nerve, whilst still cut off from its centre. Experiments by Ballance and Purves Stewart have tended to confirm the idea, that the regeneration of a divided nerve occurs by a linking up between the proximal portion and a partially regenerated distal part.

Recent experiences seem to show that the nerve fibres of the proximal end still connected with their ganglion cells, after the reunion of the ends by the surgeon, do not grow out further than that indicated by the common nerve end bulbs which form in the stumps after amputation.

Experiments on nerve anastomosis undertaken from the physiological point of view, proved that an anastomosis and a return of function occurred when the proximal end of a motor nerve was joined to the distal end of another motor nerve. But there was no restoration of function when one end was motor and the other sensory.

These experiments have enabled surgeons to restore the motor supply of the facial muscles. At first the proximal end of the spinal accessory nerve was joined, but later the junction of the proximal end of the hypoglossal with the facial proved best.

Körte and Bernhard in 1902, and Ballance in 1903, were successful in restoring facial movement and in removing the ugly disfigurement caused by facial paralysis. A false claim arose that after the union of sensory nerves there might be an immediate return of sensation. This was disproved by the experiments of Richet in 1867 and was confirmed by the clinical observations of Head and Sherren.

Surgery of the Spinal Cord

A false analogy with trephining of the skull induced attempts at trephining the spine in cases of fracture. The results were as useless as fatal. After a long series of experimental and clinical observations had made advances on Galen, and had distinguished tracts and segments, and after the introduction of antisepsis, the surgery of the spine could be begun.

MacEwen's operation in 1883 was performed on a boy for the relief of pressure due to angular curvature. The boy recovered from his paralysis so well, that five years later he could walk three miles and join in games, even football.

In 1887, Horsley removed a tumour compressing the spine in a case under Gowers. Horsley mentioned fifty-six similar cases, which had remained unrelieved. A year later the patient reported that he had worked for sixteen hours at a stretch, the work involving much standing and walking. He died twenty years later from another cause.

Recently there have occurred a very large number of operations on the spine, in the hope of relieving gunshot injuries. All the knowledge accumulated by experiments and observation has to be brought to bear on a case in order to decide whether it is one suitable for operation.

The Surgery of the Brain

The differentiation by means of experiments on animals between the functions of the various parts of the brain was begun by Legallois. He traced the origin of the movements of respiration to the medulla oblongata in 1812. Magendie and Flourens between 1824 and 1842, by a course of experiments, discovered the connexions of the cerebellum and semicircular canals with co-ordination of muscular movement and the maintenance of equilibrium.

A localisation of a speech centre was attempted by clinical and pathological observations. The cases in which aphasia accompanies apoplexy caused the speech centre to be located at first in the anterior part of the brain. In 1825, Bouillaud localised it more nearly in the island of Reil, but without distinguishing the left from the right side. The left side, as the seat of the function of speech, was first fixed upon in 1836 by Dax, and his son, Dax fils, published in 1865, 365 observations identifying as the seat of the function the left hemisphere where it borders on the fissure of Sylvius, and definitely excluding the right side. In 1861, a paper read by Aubertin to the Société d'Anthropologie, in confirmation of the observations by Dax, attracted the attention of Broca, the secretary of the Society. Broca set to work to localise the centre more nearly still in the convolution which gained his name. But the brain of Broca's first case is preserved in the Musée Dupuytren, and in 1906 Marie objected that the apoplectic lesion could be shown to have been much more extensive than that described by Broca. However, Broca's conclusion obtained acceptance at the time and undoubtedly served as a stimulus to further inquiry by experiment.

The method of experiment which was instrumental in starting the modern surgery of the brain was that of noting the result of stimulating the surface of the various convolutions of the cerebrum. In former times the convolutions had been looked upon as just as undifferentiated as the coils of the small intestines; indeed the two were sometimes treated as alike.

The localisation of the sensorimotor areas on the cortex of the dog was begun in 1870 by Fritsch and Hitzig; they used an electric stimulus, such as could be borne upon the tip of the tongue, with which they mapped out five centres about the crucial sulcus on the upper surface of the dog's brain.

Ferrier began his researches at the West Riding of Yorkshire Lunatic Asylum, with the object of putting to experimental proof Hughlings Jackson's views on epilepsy, chorea, hemiplegia, and on the "destructive" and "discharging" lesions of the grey matter of the hemispheres.

All previous experiments, involving the making of destructive lesions, had been complicated by sepsis and hæmorrhage. Lister's antiseptic method was adopted, between 1878 and 1880, by Gerald Yeo for Ferrier. He removed portions of brain from twenty-six monkeys, and in twenty-five there were no inflammatory complications. Besides the actual discovery of cerebral functions, these experiments had far-reaching results. Not only did they demonstrate the necessity for antiseptic precautions when experimenting on animals, but they were cited as evidence of the necessity of performing trephining operations under Lister's precautions, at a time when there were surgeons who ignored them.

Ferrier mapped out the cortical areas on macaque monkeys. Schafer and Horsley, then Horsley and Beevor, followed with what they called a minute analysis. Their results were plotted out on paper ruled in millimeter squares. Subsequently they compared with the above the results, that of exciting the cortex of a young orang-outang. On its brain they found intermediate non-excitable areas, such as had been asserted for man, in contradistinction to the cortex of macaque monkeys, in which the excitable areas had been found to be continuous. In addition to the cortex, the region of the internal capsule was examined, also the clinical and pathological observations which had been made on cerebral tumours were carefully correlated with the results of their experiments by Beevor.

In order to bring the results of experiment into closer relation with the function of the human brain, Sherrington and Grünbaum added experimental observations on chimpanzees, also on a gorilla.

A fundamental experiment was made by Goltz in 1892. He succeeded in removing so much of the cerebrum from dogs as to reduce the animals to the state of some of the patients confined in lunatic asylums. The experiments thus threw light upon the restricted functional activity of such patients' brains.

The experiments of Flourens on the cerebellum and semicircular canals were reviewed and their bearing explained by Hughlings Jackson in 1877 and by Bastian in 1886; these physicians co-ordinated the experimental results with clinical and post-mortem observations. Experiments in advance of those by Flourens were carried out and described by Luciani in Italy in 1884, also in this country by Ferrier and Turner, Horsley and Risien Russell, and by Sherrington. These experiments suggested improvements in diagnosis not only in connexion with the cerebellum itself, but also furnished means of diagnosing the affections of the internal ear, aided by the special tests described by Báráni.

Trephining had been practised from prehistoric times for the relief of injuries to the head, with but little change in the method of operating from that described in the works of Hippocrates and by Celsus. Saucerote in 1732 had by means of experiments on dogs introduced the subject known as "Contre Coup," in which the injury within the skull occurs at a point distant from the injury. The classical case is that of King Henri II. of France, who whilst jousting was struck over the eyebrow by his opponent's lance and fell on the back of his head. The attention of a number of medical attendants was directed to the external injury, but after the King's death there was found a suppurating blood-clot underneath the occipital bone.

Percival Pott in 1760 advocated trephining for the abscess under the skull which followed scalp wounds.

M. Petit in 1732 had sought to differentiate the concussion which caused immediate unconsciousness from the unconsciousness coming on sometimes after an accident, the result of subcranial hæmorrhage. But neither Sharp nor Pott recommended trephining under that circumstance. Abernethy attributed the case in which the onset of unconsciousness was delayed to a rupture of the middle meningeal artery; but Charles Bell took an opposite view, saying that the dura mater was separated by the blow, and the collection of blood was a secondary matter.

Toward the end of the eighteenth century trephining fell into disrepute, especially in France, and during the first part of the nineteenth century the operation almost ceased to be performed.

The cases referred to by Astley Cooper either died or recovered without being trephined. Instead they were subjected to large venesections, purgings and salivations.

Stromeyer, a foremost German surgeon, in an address at St. Thomas's Hospital in 1874, advised that even in depressed compound fractures, the fragments should be left to become loosened by suppuration. Walsham, a surgeon to the same hospital, a hundred years after Percival Pott, published a paper in 1881 with the apologetic title, "Is trephining the skull a dangerous operation *per se?*"

The explanation why trephining was opposed is to be found in the septic state of the great hospitals.

In the country outside of the infected atmosphere of the great hospitals trephining was more largely and more successfully practised. Thus in the neighbourhood of the mining and blasting works around Redruth and Camborne in Cornwall, it was reported that, at any time, and without any trouble, more than a score of men could be interviewed who had been trephined. One surgeon at Redruth had a collection of sixty-four pieces of the skull removed by trephining, and another surgeon had between forty and fifty specimens. Those who opposed trephining declared that such trephining had been done unnecessarily.

The fresh start in the application of surgery of the brain was made under the guidance of the results of experiment and the employment of the antiseptic method. MacEwen in Glasgow, in 1876, made a correct diagnosis but operation was refused; after death he trephined the skull over the situation diagnosed as the site of the disease and correctly exposed it. In 1879 he removed a gummatous mass from the dura mater of a woman, and the woman died eight years later from Bright's disease. Durante in Rome in 1881, and again MacEwen in Glasgow in 1883, removed similar masses from the dura mater.

The knowledge gained by experiment was applied to the exact diagnosis of a *tumour of the brain itself* by Alexander Hughes Bennett, Physician to the Regent's Park Hospital for Nervous Diseases and to the Westminster Hospital. Bennett demonstrated that the patient presented the signs of a tumour affecting the area of the cortex on the left side of the brain connected with the right arm and situated about the middle of the fissure of Rolando. He further put his finger upon the spot overlying the tumour. On November 15th, 1884, Godlee trephined and found the tumour exactly underlying the spot which had been indicated by Bennett. On exposing the cortex, all that could be noticed was a slight elevation of the ascending parietal convolution immediately behind the middle of the fissure of Rolando. The tumour was exposed one inch under the cortex and consisted of a large glioma the size of a walnut. The patient at first progressed fairly, but there was some suppuration, and a hernia cerebri protruded through the centre of the crucial incision. Septic complications connected with the hernia caused the patient's death thirty-eight days after the operation.

A great step in advance was made by Horsley, who commenced to operate at the Hospital for Nervous Diseases, Queen Square, on May 25th, 1886. At the Brighton Meeting of the British Medical Association in the following year, 1887, he described three successful cerebral operations—an excision of a scar for traumatic epilepsy, a tuberculous tumour removed from the thumb area, and the removal of a splinter of bone surrounded by a cyst. The operations had been done under strict antiseptic precautions; a semilunar flap, the value of which he had learnt by animal experiments, replaced the traditional crucial incision.

Horsley's fifth case of cerebral operation was the removal of a glioma from the arm area of the right side which weighed 4½ ozs.; the patient died six months later from recurrence.

In order to avoid the danger from shock caused by the removal of the skull, which is particularly obvious when experimenting on animals, Horsley introduced the method of operating in two stages; the actual operation on the brain following some days later.

The *cerebral abscess* caused by ear disease had always ended fatally, except in the case of a few, in which the abscess ruptured externally and set up a persistent sinus. Morand in 1768 reported some cases in which the opening of such sinuses had been enlarged. In one case he cut through the dura mater, let out pus, put in a tube, and the patient recovered.

The first operation by MacEwen for a temporosphenoidal abscess was done in 1881, the patient being *in extremis;* a similar case, also too late, was operated upon by Hulke in 1886. The first case to survive was that in London under A. E. Barker in 1887, and shortly afterwards Caird in Edinburgh and MacEwen in Glasgow were successful. MacEwen's case healed in three weeks, and was exhibited twenty-four years after in good health.

In 1885, Horsley suggested that in addition to opening the mastoid antrum, the internal jugular vein should be ligatured if the suppuration had already extended to the lateral sinus. In 1887, Horsley said he had ligatured the vein in one case and cleared out the sinus; this operation was repeated by Arbuthnot Lane in 1888 and by Ballance in 1890.

Milligan and Hare were the first to operate for a cerebellar abscess in 1888, and in 1914 Milligan reported that he had operated upon twenty-seven cases of cerebellar abscess, seventeen of whom had recovered.

Decompression of the Brain

There are two definite limitations which prevent any wide extension of cerebral surgery. There is no regeneration of the highly-organised brain substance, and therefore any gap can only heal by scar tissue, which is essentially a diseased tissue. Further, no part of the brain substance can be lost without the patient suffering from that loss; compensation by other parts of the brain is limited. Surgeons have often expressed themselves as believing that brain matter can be lost without harm. It is a most superficial and erroneous assertion, and can only be made by those who disregard the after history of patients, and who ignore the results of experiments on animals involving the removal of parts of the brain. A tumour which compresses the surface of the brain, or an encapsuled tumour which has merely separated the substance of the brain, can be shelled out and leave the brain unharmed. The question whether a glioma or other infiltrating malignant tumour should be excised from the brain must be generally answered in the negative.

The restricted indications for the excision of cerebral tumours was well set forth in 1913 by Tooth in his retrospect of the surgical treatment of cerebral tumours at the National Hospital for Nervous Disease. Not only is there the loss of brain, but the operation appears to excite a rapid extension of the malignant disease to the rest of the brain. Left undisturbed, a glioma often pursues a very slow course.

Hitherto decompression had been limited to trephining for injury. Horsley operated for the first time with the object of relieving the patient from threatened blindness in January 1887.

The increased importance of the study of Intracranial Pressure, or Tension in relation to operations for decompression, gave an impulse to a renewed series of experiments. The effects on the pulse and respiration when the intracranial pressure was increased were noted. Some of the results were published in the *Philosophical Transactions* by Horsley and myself, and the effect especially on respiration formed the subject of my Arris and Gale Lectures in 1894. The relation between intracranial pressure and the circulation, including the influence of gravity, was the subject of important experiments by Leonard Hill.

The Pituitary Body and Acromegaly

Pierre Marie in 1886 described the condition known as Acromegaly, which is the result of disease of the pituitary gland. In that year Horsley began experiments on dogs in order to find out the best way of relieving the condition. Using a trephine with a long shank, he removed the pituitary gland of the dog through the palate, also through an opening in the temporal bone. At a later date he undertook another series of experiments with Handelsmann on twenty-three cats, twenty-one dogs, and thirteen monkeys. As the opening through the temporal bone offered the best way of ensuring asepsis, Horsley chose that method for operating on patients, doing the operation in two stages. He operated for the first time in April 1904, and in 1906 he had done so on ten patients. Three out of the first four patients survived the operation, the fourth dying without recovering consciousness. Among the ten operations there were two deaths. In 1906, Schlosser commenced the operation of reaching the gland through the nose. Further experiments were made by Cushing in 1910.

Complete removal of a pituitary tumour is out of the question, but relief follows from decompression.

EPILEPSY

Over the grave subject of epilepsy there reigns disappointment. It is a subject upon which numberless experiments have been made. Horsley and Kocher both hoped that if general epilepsy were brought about by disturbance of intracranial tension, it might be relieved by a decompressing operation. Except for the focal Hughlings Jackson type, trephining for epilepsy has generally failed. Treatment continues to be indirect, the narcotising of the brain in a hope that rest may lead to a restoration of tonic equilibrium.

There is urgent need for further animal experimentation, *e.g.* to test the prevailing biochemical theories of the causation of epilepsy.

THE SURGERY OF THE THYROID GLAND

It cannot be said that the thyroid gland was distinguished from other glands in the neck until Vesalius described and drew the gland in his *Fabrica* in 1543.

Galen had defined bronchocele as a swelling partly formed by air and partly by mucus. Probably he had in mind the laryngeal air sacs of monkeys; at any rate he did not connect a bronchocele with the thyroid gland, and, in accordance with the name he used, it was treated by following writers as a hernia-like swelling connected with the windpipe.

Jean Riolan in 1649 was the first to demonstrate that goitre was connected with the thyroid gland.

Von Haller in his *Elementa Physiologiæ*, by a process of exclusion, decided that a peculiar fluid was elaborated by the gland which passed into the radicles of the veins and so into the blood.

Little attention was paid to the thyroid gland and its real functions remained unknown. Astley Cooper named it as one of the subjects for his prize. But when in 1873 Gull, and in 1877 Ord, noted cases of what we now call myxœdema, there was no clear idea that they were describing a disease of the thyroid gland. Ord in 1883, in his article in Quain's *Dictionary of Medicine*, merely mentioned the thyroid gland with other organs as undergoing atrophy; he regarded myxœdema as a disease without remedy and the prognosis as wholly unfavourable.

After the introduction of general anæsthesia and of antiseptics, Swiss surgeons began to operate freely for goitre, and in doing so completely removed the thyroid gland. The result was that they set up a traumatic myxœdema, which was named by Kocher *cachexia strumipriva.* If the operation was done on a boy, growth was stopped and the boy became a cretin. It induced experiments on various animals with differing results, about which this explanation may be given, that in varying degrees the whole of the thyroid gland tissue is not concentrated in the anatomical thyroid gland; especially in young animals accessory thyroid gland tissue is found at the root of the neck and in the anterior mediastinum. A Committee of the Clinical Society of London was set up, of which Horsley was secretary, and he conducted experiments on monkeys. The monkeys were adults, and the thyroid gland tissue in them was, as in man, generally found concentrated in the thyroid gland. Hence he obtained definite results. Schiff had in 1884 proved that grafting in of a thyroid gland arrested the traumatic myxœdema consequent on removal of the thyroid gland from an animal. Also Schiff hinted at the administration of the thyroid gland which was introduced by George Murray in 1891. Subsequent experiments by Gley and others have dealt with the parathyroid glands. McCarrison has proved that goitre is caused by contamination derived from the fæces of goitrous patients. Farrant has in an extensive series of experiments distinguished certain diseases which start changes in the thyroid gland.

The grafting of the thyroid gland should be made the subject of further experiments.

RENAL SURGERY

Experimental nephrectomy was first accomplished by Zambeccari in 1680. With the knowledge that a dog might have only one kidney, and yet be perfectly healthy, he removed a left kidney through an incision in the loin, but the animal died of peritonitis six days later. In his second experiment he excised the kidney after tying the ureter separately from the artery and vein. The wound had healed on the sixteenth day; many months later the dog was feeding well and had become fatter. Six other dogs recovered from the operation, three permanently, three died weeks afterwards, apparently from late trouble around the ligature. Experimenters who followed noted that when the animal recovered the remaining kidney increased in size and weight.

In 1869, Simon cut out one kidney from fifteen dogs under the combined advantages of antisepsis and anæsthesia; all lived. This led him to undertake the first definitely-planned nephrectomy. A woman, forty-six, after being operated upon for a left ovarian cyst, had had for eighteen months a persistent ureteral fistula. Both a plastic operation and the application of the cautery having failed, the kidney was removed through a retroperitoneal lumbar incision. The woman recovered, and was able to help in the Military Hospital in July 1870. She afterwards returned to her house work, and was well seven years later.

Since then there have been other experiments which have produced results important for surgery. Of these two may be mentioned.

The excretion of colouring matter by the kidney is noted in the *Philosophical Transactions* for 1757. The prickly pear of Carolina, *Opuntia*, when eaten caused the urine to turn a milky red, indigo swallowed caused the urine to turn blue. Experiments from the physiological standpoint were undertaken by Chrzonsczewsky of Kazan in 1862 and by Heidenhain in 1875. By injecting indigo carmine into the jugular vein of animals it was found that the colouring matter was excreted by the activity of the cells of the tubules. In 1903, Voelcker and Joseph applied this discovery to the purpose of estimating the activity of the kidneys, and as a means of recognising the degree to which their secreting power had been destroyed by disease.

In 1909, Rowntree and Gerachty, as the result of a number of carefully devised experiments, selected phenolsulphonephthalein. When this innocuous colouring matter is injected under the skin of the arm, a pinkish tinge begins to appear in the urine within a few minutes, if the kidneys are fully active. If there is a delay for twenty or thirty minutes, a grave impairment of the functional activity of the kidneys is indicated. A 6 mgm. dose of the colouring matter should be completely eliminated by the urine within two hours; defective kidneys fail to excrete half within that period.

Rose Bradford's Experiments of Partial Removal of the Kidneys.—A particularly insidious impairment of the kidneys is marked by a fall in the specific gravity of the urine below 1010, at the same time that there is an increase to double the quantity in the urine passed. The condition is often produced by an enlargement of the prostate. It may be confirmed by the colour test just referred to, but is explained by Bradford's experiments on dogs which he made in 1895. He first excised a wedge from the middle of a kidney of a dog and united the two poles by suture. At a subsequent operation he removed the whole of the opposite kidney. He thus reduced the total of the dog's excreting kidney gland tissue by two-thirds or three-fourths. When the total kidney substance was reduced by about two-thirds, the animal passed a greatly increased amount of urine, of low specific gravity, but remained in fair health. When the kidney tissue had been reduced by about three-quarters the animal not only passed dilute urine, in a greatly increased amount, but this was accompanied by emaciation which soon ended in the death of the animal. The blood and muscles of the dead animal contained a large excess of nitrogenous extractives. The experiment suggests a loss of internal renal secretion, which normally controls tissue waste. A patient whose urine corresponds to the state illustrated by these experiments is in a state of chronic uræmia; the prognosis is grave and any operative interference hazardous.

SEPTIC ORGANISMS

Demonstrations of the Infection of Wounds by Micro-organisms.—Tradition presented an enormous barrier against any novel doctrine as to the cause of wound infections—infection of the hands in dissecting and in making post-mortem examinations, such as happened to anatomists, to Spigelius and to Perrault, suggested Haller's experiment. He made a watery extract from dead bodies which poisoned animals, but that did not make him change from the traditional belief that wounds were infected by foul air. Orfila, in 1808, extended Haller's experiments by showing that the blood of the animals, into which the so-called cadaverin had been injected, when introduced into other animals poisoned them also. Magendie in 1823 repeated these experiments and produced both septicæmia and metastatic infections, pyæmia. Cruveilhier in 1836 showed how this was brought about by blood clotting in the veins and then suppurating. Virchow elaborated this and described how the suppurating clot broke down in the veins and formed emboli. But this was then held to be a chemical catalytic process. When Pasteur commenced his researches on fermentation, the chemists in particular were united in rejecting organisms as the cause of fermentation.

Pasteur, following upon his discovery of the cause of alcoholic and lactic acid fermentation by living organisms, discovered in 1862 the vibrios in decomposing albuminous fluids which developed at the same time that foul gases were given off. On animals the fluid containing the vibrios acted as a deadly infection, however much the fluid was diluted. Since it caused fatal septicæmia, he gave the organisms the name of "microbe septique."

When, however, blood drawn off from a dog was heated at intervals in a flask, decomposition was prevented. This experiment was first made between April 3rd and 20th, 1862. The opponents of Pasteur, including Billroth, continued to advocate a catalytic explanation; Panum of Copenhagen advanced in favour of this, that when an infusion of meat was boiled for eleven hours and then distilled, the distillate proved as poisonous as the original infusion. He and Billroth really experimented with toxins derived from micro-organisms.

It was at this stage of discovery that Lister began his antiseptic method; it was founded on Pasteur's researches on fermentation, and his primary aim, therefore, was to prevent infection from the air.

The next step was made by Chauveau in 1873. The extravasated blood resulting from the method of castration known as bistournage normally remained in the scrotum uninfected. Chauveau took the supernatant fluid from standing pus and injected it at the site of the bistournage. This started suppuration in the blood clot.

About the same time there was a discussion in the Académie de Medécine, when some said that disease was engendered by ourselves within ourselves, and generally the germ theory was condemned, including the measures suggested by it. Pasteur, on the other hand, declared that anthrax is a disease produced by the bacterium, as trichinosis by trichina, as itch by the acarus, but with this difference, that the anthrax parasite can only be seen through a microscope of high magnification. Wilks told the story of a meeting at the Pathological Society where a member having mentioned the word bacteria, a well-known physician asked Wilks what connection the disease had with frogs (batrachia).

In 1872, Klebs described the micro-organisms which he had found in gunshot wounds. But the difficulties in isolating and distinguishing various organisms had not been overcome, and numerous claims were made which gave opportunities for ridicule by opponents. Anthrax continued the organism most suitable for experiment, and Koch in 1876 demonstrated its spores, and Pasteur in 1877 the spores of the hay bacillus.

The discovery of the two chief pyogenic organisms was begun by Pasteur. From a boil on a laboratory assistant Pasteur obtained staphylococci, also he obtained the same organism from the pus of acute osteomyelitis. He then declared that the same organism produced both affections—"osteomyelitis is the furuncle of bone." In 1880, Ogston found the same organism in acute abscesses, and the pus being injected under the skin of a rabbit, an abscess was produced containing the same organism. But he did not always find the organism in chronic abscesses.

In 1878, Pasteur was present when a speaker was enlarging upon the causes of epidemics in lying-in hospitals. Pasteur intervened and said: " None of those things cause the epidemics, it is the nursing staff and medical staff who carry the microbes from an infected woman to a healthy one." When the speaker retorted that he feared the microbe would never be found, Pasteur went to the blackboard and drew a diagram of the chain-like organisms, saying, " There, that is what it is like." Visiting a lying-in hospital, Pasteur pricked the finger of a woman suffering from puerperal fever, and demonstrated the streptococcus in the blood.

Koch depicted it under the name of the Chain Coccus; Billroth called it Streptococcus.

In 1882, Fehleisen of Wurzburg saw streptococci in the lymphatic spaces of the skin and subcutaneous tissue of patients upon whom erysipelas had been inoculated. With the object of relieving malignant disease, he inoculated patients with erysipelas and observed the same micro-organism in the inoculated. Eschweiler in 1898 found that the serum of an animal which had been rendered refractory relieved erysipelas and thus the streptococcal antitoxin came into general use.

Burdon-Sanderson's article on the "Pathology of Inflammation" is a most important contribution to the history of the subject from 1870–1880.

Lister's antiseptic method received its fullest measure of acceptance at the International Medical Congress held in London in 1881. After that a further series of experiments caused its replacement; in contradistinction to "antiseptic," the method which replaced it was called "aseptic." Both terms are but names.

In Germany carbolic acid, as the chief antiseptic, was replaced by mercuric chloride. This was based on Koch's experiments, described in 1881, of the way in which anthrax bacilli in glass cultures were killed by solutions of corrosive sublimate. As a matter of fact, the experiments were not to the point; the real question related to staphylococci and streptococci in living tissue, not to anthrax bacilli in glass cultures. As an antiseptic, mercuric chloride was as harmful to living cells as carbolic acid, if not more so.

Therefore experiments were directed to getting rid of the use of antiseptic solutions which did harm to living cells.

In 1878, Pasteur recommended the sterilisation of instruments by flaming them, the sterilisation of tow, pads, dressings and bandages by moist heat under pressure at 130° C.

to 150° C., and of water by boiling under pressure at 110° C. to 120° C. The use of such apparatus was combined with a system of careful cleanliness.

Neuber in Kiel commenced in 1882, in a special hospital, a search for micro-organisms in everything connected with a surgical operation, and he obtained sterility by boiling instruments, dressings, also the clothes of patients and attendants; antiseptic solutions were replaced by the washing out of wounds with boiled salt solution.

Schimmelbusch, in von Bergmann's Klinik in Berlin, was the chief one to popularise the procedure, and a demonstration was given at the 10th International Congress in Berlin. Use was made of the bacillus pyocyaneus as an indicator to the naked eye of the growth of micro-organisms.

Schimmelbusch did not, however, include the mention of gloves. Sterilisation of the surgeon's hands proved to be a difficulty, whether under the antiseptic or aseptic system; the most satisfactory solution was found in the wearing of the rubber gloves, introduced by Halsted in the United States in 1891.

Two further sets of experiments have had an important bearing on surgery.

In 1907, Dudgeon and Sargent distinguished between the staphylococcus pyogenes aureus and the staphylococcus albus. Whilst the former was a principal source of infection of wounds, staphylococcus albus was found in healthy tissues, and in wounds healing by first intention. It was an organism which was kept in check by the cells and fluids of the healthy body, and that so long as the cells of the tissues were not injured or the fluids subjected to decomposition. Hence it has become the surgeon's object to prevent destruction of cells and decomposition of fluids in order that wounds may heal by first intention.

A series of experiments made by P. L. Friedrich in 1898 were ignored as completely in Germany as elsewhere, although the experiments pointed out the importance of excising a freshly-infected wound. Indeed the experiments by Friedrich have the merit of an elementary demonstration. They anticipated a great advance made by surgery during the War.

Friedrich cut into the musculus triceps brachii of the guinea-pig and inserted a little garden mould or room dust, then the incision was sewn up. This inoculation caused the death of the animal from acute gas gangrene and suppuration, on an average, in fifty-four hours if garden mould were inoculated, in forty-five hours if dust from a room. Bacteria were found in the outer parts of the triceps muscle in eight hours from the time of inoculation, and in internal organs in ten to twelve hours.

If the margins of the wound, including the edges both of the skin and muscle, were freely excised within six hours, and the wound again sewn up, the animal remained sound. If the excision were done between six and eight hours from the time of inoculation, the result was uncertain. Some of the animals remained unharmed—some died of gas gangrene. If the excision were done after eight hours, the animals invariably died. If within six hours of the inoculation by room dust, the wound was excised and the excised portions used to inoculate a second guinea-pig, the second guinea-pig died on an average in twenty-three hours, instead of forty-five hours. This demonstrated that in the first animal the organism had developed greater virulence than when in the original dust. The bearing of this last point is this, that some experimenters have used organisms for inoculation which have been cultivated beforehand to a virulence in excess of the natural. Thus Schimmelbusch inoculated the tails of mice with virulent anthrax cultures, and found that the cutting off of the tail after ten minutes failed to save the mice from dying of anthrax.

But experiments with such virulent cultures produces an unduly pessimistic view. The general run of organisms have a latent or incubation period during which they do not spread beyond the margins of the wound. Excision of the margins of the wound during that incubation removes the infecting organisms, and the wound can then be sutured. Comparing this with the antiseptic method, even granted that antiseptics come in contact with and kill the infecting germs, there is so much destruction of the cells and tissues of the edges of the wound, that the wound cannot be closed. Being left open, there is an opportunity for re-infection.

ANTHRAX

Anthrax in Greek, carbunculus in Latin, is the word for charcoal, then for the ruby or garnet, then for a burning gangrenous sore on the skin, in which perhaps smallpox and plague sores were sometimes included. The restriction of the term anthrax to the specific disease began in France. Saporta, who was Professor of Medicine at Montpellier, and who died in 1573, stated in his work on tumours that there was a form of carbuncle which frequently attacked butchers and their families owing to contagion from the skins and offal of diseased sheep. The country people called the disease "La Marrana." Larrey, whilst practising in Paris during the Revolution, noted several instances of anthrax which occurred in the family of a butcher; one man had a malignant pustule on the left cheek and another in the neck; both were untreated and died. The butcher's wife developed a malignant pustule on the left cheek which Larrey cut out and applied caustics to the wound. She recovered, the wound healing in six weeks. This treatment by Larrey may be said to have started the practice of excision. The first account of malignant pustule in this country is to be found in South's translation of the *Surgery* by Chelius, 1847, I., 63. The notes by South include reference to the literature, also to three cases under Lawrence at St. Bartholomew's Hospital. Lawrence's first case, in 1825, was inoculated on the eyelid from the leather with which he worked, the other two were employed in a horse-hair manufactory, and presented a pustule on the chest and forearm respectively. All three were mild cases and recovered — the first was cut into, the other two sloughed out spontaneously. On the other hand, there were severe infections—thus Budd of Bristol, at the British Medical Association meeting in London in 1862, reported fifteen cases, all fatal, except one, the recovery of which was attributed to early incision and cauterisation.

The cutting out of the pustule was practised here, especially at Guy's Hospital. The excision produces a painful, slowly-healing wound, after which there remains on the face or neck an ugly scar. But further experience has shown that in mild cases excision errs by excess, and in virulent cases is useless. In cases moderate in virulence excision, as also cutting into the pustule and applying caustic, may fail, not only because some germs are left, but because the surgical procedure interferes with the protective zone which forms around.

Improvements in medical treatment have afforded not only a better way of saving life, but under it the site of the infection disappears and leaves hardly a trace.

The identification of the cause of anthrax proved all the easier because of the size of the bacillus. In 1838 Delafond at Alfort saw little rods in the blood of infected animals, as also did Pollender in 1849, and Davaine and Roger in 1850. But no importance was attributed to the observations until after Pasteur's publication. Then, in 1863, Davaine recalled his earlier observations and termed the rods bacteria. Pasteur's difficulty at first was to distinguish between the infection through the blood by the anthrax bacilli from the concurrent infection by septic organisms. This he accomplished in 1877 when he demonstrated to the Académie de Médecine that the anthrax bacilli were ærobic, the septic organism anærobic. In 1878, Pasteur declared that the spread of infection among cattle was through the soil, especially by means of the worm casts to which Darwin's observations on earthworms had drawn attention. At the International Medical Congress in 1881, Pasteur stated that in February of that year he had inoculated sheep with an attenuated virus from anthrax cultures and had so protected the animals against subsequent inoculations of a virulent virus. Upon this followed trials of the specific serum drawn from immune animals, as a means of arresting the progress of the disease in man. At first this serotherapy had only a limited success, until in 1895 Sclavo, Professor of Hygiene at Siena, found, after experimenting on various domestic animals, that a more active specific serum could be derived from an ass which had been rendered immune to anthrax.

By a further series of experiments in 1917, Kraus at Buenos Ayres discovered that simple bovine serum, administered freely and early, produced an effective reaction. He reported one death among 146 cases of cutaneous anthrax, treated solely by the intravenous infusion of the above non-specific serum of the ox.

Rabies and Hydrophobia

The mad dog and the disease transmitted by its bite were both well known to the ancients. Xenophon and Aristotle refer to the subject, and Apuleius included a mad dog incident in his *Metamorphoses.*

For one bitten by a mad dog Celsus recommended cupping over the bite, also sweating in a hot bath and by drinking wine. For a man attacked by hydrophobia there was one special measure, the patient should be thrown into a water tank and submerged until he was forced to gasp and swallow water. But he might then become convulsed, and should be transferred at once to a bath of warm oil. A rationalising explanation of the above is that hysterical cases had been cured in that way. In face of the terrible suffering incident to hydrophobia, it became common in some countries for those afflicted with hydrophobia to be killed, as if a dog or wolf, shot, poisoned, strangled, suffocated. As late as 1819 in France a patient suffering from hydrophobia was smothered between two pillows.

To the *Philosophical Transactions*, in the middle of the eighteenth century, there were three notable contributions.

Nourse, in 1738, described the case of a lad bitten by a mad dog through the nail of the right thumb who died of hydrophobia nineteen months later. The boy aged sixteen was bitten in June 1735; the bite was cauterised at once and healed. In the summer of 1736 he was cut for stone and was about again in five weeks. On January 11th, 1737, he complained of numbness in three of the fingers of the left hand, followed by pain in all his bones and across his stomach, symptoms of hydrophobia developed and he died within forty-eight hours from the first onset of the symptoms.

In 1891, in conjunction with Horsley at the Brown Institution I was able to give a complete proof that a child had died from hydrophobia two years and four months after being bitten by a mad dog. The child's first complaint of pain was in the scar left in the skin of the popliteal space by the puncture of the canine tooth of the dog which had been proved at the time to be rabid. Freyer, in 1919, reported a case in which the incubation period had been eighteen months.

In 1744, Ranby gave a very full account of a case of hysterical hydrophobia lasting weeks, followed by a sudden and complete recovery.

In 1750, Starr of Liskeard reported the case of a horse bitten by a mad dog on its shoulder. The wound healed and the horse was ridden short journeys until the twenty-fifth day, when on being taken to a pond to drink the horse trembled and could not drink; on being taken back to the stable it ate some oats and hay; that night it bit at the scar and at the manger, and the next day an attempt to drink caused spasms. Subsequently the horse kicked his stall down and was covered with blood before it was shot.

A precisely similar case happened in the Brown Institution to a mare bitten on its muzzle by a mad dog. It kicked its stall to pieces and was covered with blood before it could be got at to be destroyed.

Pasteur, when a boy in October 1831, had experience of the terror produced throughout the Jura by the invasion of a rabid wolf which went about biting men and cattle. He saw one man cauterised at the smithy near his father's house, but eight persons bitten on the hand or head in his neighbourhood died of hydrophobia after horrible suffering. For years the district was in dread of that mad wolf as if it had lived. It is needless to recall the wholly useless methods of treatment which were tried.

In 1880, Pasteur took up the study of rabies and hydrophobia with two mad dogs brought to the laboratory, one animal suffering from dumb rabies. The minority of cases which took a paralytic course from the first were a source of much confusion. Instead of the symptom characteristic of hydrophobia, animals and patients suffered from acute ascending paralysis such as was described by Landry in 1859. The Brown Institution laboratory attendant who accompanied Horsley to Paris, died there of the "dumb rabies" type of the disease.

On December 10th, 1880, a child aged five died at the Hôpital Trousseau under Lannelongue after a bite on the face a month before. Four hours after death Pasteur took some mucous from the mouth and inoculated rabbits which died within thirty hours, and their saliva inoculated into other rabbits provoked an almost equally rapid death.

After various experiments Pasteur selected the medulla of a mad dog and thus obtained a material free from the septic germs contained in saliva or wound discharges. The mixed infections resulting from previous experiments had prevented the two diseases from being separated. By making an emulsion of the medulla in glycerin and inoculating the material into the subarachnoid space over the convexity of the cerebrum of rabbits, Pasteur arrived at constant results. The incubation period became fixed at seven days. Starting from this fixed virus, he obtained definite degrees of attenuation by drying the medulla.

Commencing with the most attenuated virus and repeating the injection with an increasing strength of virus, Pasteur succeeded in making dogs refractory to inoculation of the fixed virus. He described the results of his experiments at the Copenhagen International Medical Congress in August 1884.

He first adopted this method for rendering a human being refractory during the incubation period in the case of Joseph Maître, aged nine, who had been bitten badly on the arms and legs. The preventive treatment was begun on July 4th, 1885, and five years afterwards the boy was alive and quite well.

The success of Pasteur's preventive treatment was extraordinary. Of the first 350 patients only one died, a little girl who had been horribly bitten about the head and face thirty-seven days before being brought to Paris. The marvellous results have continued and hydrophobia rapidly disappeared from countries, except where wolves and jackals keep up the disease. It soon dies out in foxes and cats. The Act of Parliament enforcing muzzling for a time and quarantining of dogs at the port of entry was carried by the energy and resolution of Mr. Walter Long.

The re-introduction of the disease has been due to the ignoring of the quarantine regulations, and by a lack of resolution on the part of the Government. Practically the incubation in animals is always short, all the evidence goes to show that it is under forty days. The incubation period in human beings may be very much longer.

The story of rabies is the more remarkable seeing that the present stage has been reached without the organisms causing the disease having been discovered.

The scientific treatment introduced by Pasteur did away with that necessity for cutting out and cauterising the site of the bite, which had proved wholly inadequate to arrest the fatal onset of hydrophobia.

DIPHTHERIA

In the middle of the seventeenth century, Severino, in connexion with the epidemic of Angina (presumably diphtheria), in Naples, declared that tracheotomy was the sovereign remedy, although he added there were many apparently recovering who died of collapse. Passing over a period of confused and unsuccessful practice, in 1868 Trousseau adopted Bretonneau's idea of diphtheria as a specific infection, and he encouraged the performance of tracheotomy in particular cases. In the course of five years at the Hôpital des Enfants Malades in Paris there were 215 cases of tracheotomy, with 47 recoveries, *i.e.* in 21 per cent. of the cases in which tracheotomy was performed.

Before the experimental researches which led to the earlier diagnosis and the serum treatment, I do not think that the recovery following tracheotomy in English Hospitals (tracheotomy was nearly always done late) exceeded one in ten.

The first to find micro-organisms in the diphtheritic membrane was Klebs in 1875.

In 1882, Lœffler distinguished a rod-shaped organism which he separated, and he inoculated it upon the tracheal mucous surface of animals and pigeons after the mucous layer had been first scratched. The characteristic membrane was formed; none of the other micro-organisms in the diphtheritic membrane did this. The other important point was that the bacilli were only to be found at the seat of the inoculation.

In 1888, Roux and Yersin filtered cultures of the bacilli, and the toxin freed from bacilli was found capable of producing paralysis in animals.

Upon this, in 1890 von Behring and Kitasato by injecting serum taken from an infected animal, produced in the second animal a degree of immunity to the inoculation of diphtheria. In 1892, von Behring had succeeded in arresting the disease in an animal suffering from diphtheria, and in 1893 he reported the first cases of human diphtheria treated by antitoxin.

By the beginning of 1894 Roux had made several horses immune, and the commencement of treatment with serum from immune horses was begun at the Hôpital des Enfants Malades on February 1st, 1894.

Between 1890 and 1893 the average mortality among 3971 cases of diphtheria at the Hôpital des Enfants Malades and at the Hôpital Trousseau was 51 per cent. In the four months after the commencement of the antitoxin treatment at the Hôpital des Enfants Malades it fell to 24 per cent. Meanwhile the mortality at the Hôpital Trousseau, where antitoxin was not used, had risen above the average of the five previous years to 60 per cent.

The serum treatment has entirely changed the application of surgery to diphtheria; tracheotomy has become called for only in the few cases in which the serum has not been administered soon enough. For many cases in which there is laryngeal spasm rather than an obstruction by membrane, intubation without the need of an external incision suffices.

During the recent War the question of the diphtherial infection of wounds and sores was raised. After full inquiry a solution was found by the discovery of "carriers" suffering from latent infection of the fauces by the true bacillus of Lœffler as identified by animal experiment.

TETANUS

From the earliest times down to 1884 the most varied states were included under the term tetanus. The ancients recognised and named the conditions of opisthotonos and emprosthotonos, but they confused the disease with trismus, risus sardonicus, spasms from nerve irritation, chorea, paralysis agitans, convulsions following acute hæmorrhage, spasms in cerebrospinal meningitis, rigors in acute fever, and the spasms due to strychnine poisoning and electrical excitation.

It was well known that tetanus might follow slight injuries. Hippocrates noted a case after a crush of the finger, John Hunter after a rusty nail had been run into the foot, Larrey after a sergeant had fallen on his nose and caused a slight abrasion. Spencer Wells experienced the occurrence of tetanus after ovariotomy, probably set up by the ligature, and he was perhaps one of the first to distinguish between spasm due to nerve irritation and the true tetanus which he conjectured to be a blood disease. He suggested that light might be thrown upon the cause by the inoculation into animals of wound discharges, or of the blood, or of the juice of muscle, or of the urine from a patient suffering from tetanus. He did not, however, pursue the matter. No reference to such a view of tetanus is to be found in the books of that date, neither in the edition of Holmes and Hulke's *System of Surgery*, nor in Quain's *Dictionary of Medicine*, both published in 1883, nor in the edition of the *Surgery* by Erichsen and Marcus Beck, published in 1884.

Hulke merely copied from John Morgan's Lecture on Tetanus in 1833; Morgan poisoned some dogs with strychnine, which he termed artificial tetanus, and neutralised the effects by curara; his lecture, indeed, had no relation to real tetanus.

Tetanus had occurred with wide variations in war; the German statistics of the Franco-German War included 350 cases, *i. e.* 0·35 per cent. of all wounds. Tetanus neonatorum was common, and that not only in the West Indies, for at the Rotunda in Dublin, among 17,650 infants born before 1882, 2944 died of tetanus, *i. e.* 16·5 per cent.

There was no rational treatment—medical treatment was limited to administering opium and chloral; surgical treatment was not only useless but harmful—the stretching, cutting or excision of nerves, the forcible dilatation of the wound or of the urethra; amputation was a failure.

As the result of one set of experiments, the confusion which had hitherto prevailed was cleared away.

In 1884, Carle and Rattone in Turin demonstrated that tetanus was inoculable into rabbits, by inserting the pus from a patient suffering from tetanus. Tetanus had started in a patient from an acne pustule on the neck, and from one rabbit so inoculated, tetanus could be transferred to a second rabbit.

In the same year, 1884, Nicolaier found that tetanus could be inoculated into animals from earth lying under houses being pulled down in Göttingen, also from the dirt in streets and from the mould of cultivated fields. Those engaged in the above work had suffered from tetanus. Nicolaier further noted strange bacilli which were described as resembling drumsticks by Rosenbach in 1886 and were cultivated by Kitasato in 1889. Kitasato excluded air from the cultures, replacing it by hydrogen, and the culture grown in the absence of air reproduced the disease. A pure culture did not set up suppuration. A probable explanation of the failure of previous experiments is that dogs had been used, an animal refractory to tetanus, Carle and Rattone succeeding because they used rabbits.

Verneuil, in 1886, made the important discovery that horses suffer from a chronic type of tetanus, and serve as an intermediary host; the bacilli make their exit from the horse in its dung, and the spores persist in manured gardens and fields and in road earth. It was noted that tetanus frequently appeared among farm labourers and stablemen working among infected horses; it occurred twice as often among men in the cavalry, as compared with the infantry, whilst it never happened on board ship. He also noted that it occurred in horses following castration by the same veterinary surgeon; it was assumed that the instruments inoculated the disease, as had already been proved to happen in connexion with syphilis.

An insidious cause of tetanus after surgical operations was traced by Richardson to the catgut ligatures made from sheep's intestines.

In 1892, von Behring, taking advantage of the relative great resistance which can be induced in horses, commenced the serum treatment of tetanus.

The prophylactic use of tetanus antitoxin was first adopted on a large scale by French veterinary surgeons, especially to protect horses against tetanus inoculated in the course of castration. In 1912, Vaillard stated that 13,124 animals had been operated upon after prophylactic injections without the occurrence of a case of tetanus. Meanwhile two veterinary surgeons had seen 139 cases of tetanus supervening, in particular after castration, in animals which had received no prophylactic injections.

Dieudonné, in 1909, recorded 1009 operations for castration or hernia after one prophylactic dose. There had not been among these a single case of tetanus, although during the same period he had seen 87 cases of tetanus in horses after such operations or after wounds, but which had not received prophylactic injections. See also Chapelier and Huguier.

Prophylaxis against human tetanus was first adopted on a large scale in the United States in face of the number of cases of tetanus occurring owing to injuries by the letting off of blank cartridges on July 4th. In 1903, 415 cases of tetanus occurred; in 1907 it was stated that in the previous five years there had not occurred a single case of tetanus amongst those who had received one prophylactic injection.

One of the instances of unpreparedness when the late War began was the absence of a system for preventing tetanus. It is explained that as tetanus had been absent in the South African campaign, it was assumed that the disease had lost its former importance in military surgery.

The connexion of a campaign on highly manured soil with tetanus, and the importance of the prophylactic measures which the French veterinary surgeons had first proved is now evident.

VENEREAL DISEASE

An acquaintance with the history of venereal diseases discloses two chapters which excite feelings of regret, firstly, that in order to establish a distinction between syphilis and gonorrhœa, so many experiments in the first part of the nineteenth century should have been performed on human beings; and secondly, that systematic experimentation on animals should have been adopted so late. Those who contend that syphilis was brought to Europe from America by the return of the followers of Columbus, and those who hold that syphilis existed in Europe and in Asia before the discovery of America, each succeed in exposing the weakness of their opponents' case, but fail to establish by positive evidence their own case.

The outbreak of syphilis in Spain and Italy, and its spread to Northern Europe, which followed upon the discovery of America, may have been the result of connexions between Europeans and the aboriginal women of the

West Indies, a more virulent form of a pre-existing disease being induced. At any rate this view gains support from what occurred recently in Uganda.

Moreover, the outbreak in Europe was apparently complicated by being mixed with various forms of septic infection. This would explain the severity of the manifestations of primary and secondary syphilis, described by the earlier authorities.

Up to the end of the eighteenth century the sufferings from syphilis were increased by the irregular administration of mercury, at one time too much was given, at other times too little.

With the nineteenth century there was a tendency to give too little mercury, indeed some omitted it entirely.

Apart from the consequences of the abuse of mercury, in the nineteenth century the manifestations of early syphilis had become less severe, and writers, ignorant of the later pathology and complications of syphilis, were disposed to look upon it as a merely local and even trivial disease.

Numerous experimental inoculations on human beings, especially by Ricord, finally distinguished syphilis from gonorrhœa; incidentally both diseases must have been spread further by such inoculations.

Advances in the study of pathological anatomy gradually demonstrated that gummata, aneurysms, locomotor ataxia and general paralysis of the insane were indeed the later grave manifestations of syphilis, which tended to degeneration and death.

During the latter half of the nineteenth century there was no essential improvement in the treatment of syphilis. Iodide of potassium afforded relief but did not cure. Those practitioners who were on the right road in administering mercury in moderate doses over a long period had very little to guide them. The advice to continue the course for two to three years after all manifestations had disappeared, and to repeat the same should fresh manifestations supervene, was very difficult to follow. The most amenable of patients wanted to give up taking the mercury, after the outward signs of syphilis had gone. There was also great difficulty in making an early diagnosis of syphilis, and there was therefore great delay in the commencement of the treatment.

Before the commencement of the systematic experimentation on animals, Hutchinson and Fournier were the authorities generally accepted; in the light furnished by experiment, we can recognise the restricted character of their information.

The recent advance in the treatment of syphilis has been due to experiments on animals in three directions.

(1) The *discovery of the organism causing syphilis* had been preceded by several false claims. In 1905, Schaudinn, who had previously made some observations upon the parasite of tropical diseases, including trypanosomes and spirochætes, observed spirilla in fluid taken from a primary chancre. After much difficulty Schaudinn and Hoffmann distinguished from other spirilla, a particular spirillum as more constantly present in syphilitic lesions. They named it spirochæte pallida because it was like a fine hair, relatively unstainable.

The proof that the spirochæte pallida is the organism causing syphilis was arrived at by combining the above with the experiments previously made by Metchnikoff at the Pasteur Institute. In 1903 he succeeded in inoculating a female chimpanzee with syphilis. Fournier inspected the ape and declared the signs to be absolutely typical of chancre, and he gave his reasons at length. It was the first successful inoculation of syphilis into animals which he had ever seen or known of. Subsequently the inoculation of rabbits was accomplished, and rabbits were used in the testing of the arsenical compounds.

(2) *Wassermann's Serum Reaction.*

There had been a long series of experiments on animals concerning the changes in the blood brought about by various infections, and on the immunising of animals against infection. Researches on the coagulation of the blood, such as those by Bordet and Gengou concerning coagulation and anticoagulant serum, had shown that the fibrin ferment furnished by different species of animals, although having the same fundamental property, were not identical. Changes in the blood could be induced by which bacteria were destroyed, or the red blood corpuscles clumped together and then dissolved —bacteriolysis, and hæmolysis.

A practical outcome of a multitude of experiments was the establishment of a test for the presence of typhoid fever. Further experiments on similar lines by Wassermann furnished a test for the presence of syphilis in a patient. This brought about a twofold advance: the existence of syphilis could be diagnosed in a patient who presented no external manifestation of the disease, and it furnished a criterion as to the efficiency of the treatment, as well as a guide as to the necessary period over which the treatment must be continued.

The Treatment of Syphilis by Organic Compounds of Arsenic.

Laveran, in 1903, proved that the acids of arsenic destroyed trypanosomes but were not strong enough to cure the animals. The first organic compound to be tried, atoxyl, whilst not active against trypanosomes in test-tubes, killed the parasites in animals. Atoxyl, when used for relapsing fever and sleeping sickness in man, proved too poisonous.

Ehrlich, by carrying through a long research upon arsenical compounds, the compounds being synthetised and then each tested on animals (mice, rats and rabbits), produced the compounds known as arsenophenyl glycerin and dioxydiamidoarsenobenzol, which later became known, from its number among the substances made and tested on animals, as "606," or salvarsan. In this research Ehrlich was assisted by Hata and Bertheim.

Ehrlich first referred to the drug "606," or "salvarsan," as effectual against sperillosis of fowls, relapsing fever and syphilis inoculated into rabbits. In September 1909 he sent some of the material to Alt of Uchtsprunge, who reported that he had used it successfully on twenty-three cases, previously treated without effect. Alt began the treatment of twenty-seven cases of "florid" syphilis on January

31st, 1910, and reported on April 11th that fourteen had lost the Wassermann reaction. Alt's cases were all first tested by the Wassermann reaction. During the summer of 1910, the treatment by Ehrlich's remedy spread throughout Germany and the world.

These discoveries tend to remove from surgery the complications resulting from uncured syphilis; operations for aneurysms, gummata, necrosis of bone, cancer of the tongue, etc., are required less often. Conversely the discovery has facilitated the diagnosis of those diseases, which syphilis is apt to imitate.

Experiments upon Apes have shown that it is useless to excise the site of infection later than eight hours after the inoculation, and therefore the excision of a developed chancre is contraindicated.

Further experiments on animals with the organisms of syphilis may yet furnish the means of obtaining a more effectual treatment on the lines of serumtherapy.

Conclusion.

In each of the various subjects which I have selected for notice from the history of surgery, I have been able to point to a period in which no progress was made. Then through the knowledge gained by a series of experiments an important advance took place. The intimate connexion between the development of surgery and experiments on animals continues, and experiments on animals by men acquainted with the surgery of the time will have in the future important results in relation to further extensions of the art of surgery. Two conditions will make for successful results, a study of the experiments previously made upon the subject in question, and an early fostering of the talent of originality, which, in the opinion of F. M. Balfour the embryologist, must be developed before the age of thirty.

REFERENCES

ALT, K. Treatment of Syphilitic Patients with Ehrlich's Arsenical Compounds. *München med. Wochenschrift*, 1909, 1457; *ib.*, 1910, 561, 831.

BALLANCE, C. (1) Removal of Pyæmic Thrombi from the Lateral Sinus. *Trans. Med. Soc.*, Lond., 1890, **13**, 345.
(2) with EDMUNDS, W. *Ligature of the Large Arteries in Continuity*, Lond., 1891.
(3) with PURVES STEWART, J. *Healing of Nerves*, Lond., 1901.
(4) with BALLANCE, H. A., and PURVES STEWART, J. Faciohypoglossal Anastomosis for Facial Paralysis. *Brit. Med. Journ.*, 1903, i. 1009.

BÁRÁNYI. Physiology and Pathology of the Semicircular Canals in Men. *Monatschrift f. Ohrenheilkunde*, 1906, **40**, 191, and subsequent communications.

BARKER, A. E., with GOWERS, W. R. Temporosphenoidal Abscess from Ear Disease successfully treated. *Brit. Med. Journ.*, 1886, ii. 1154.

BASTIAN, H. C. (1) On the Muscular Sense. *Brit. Med. Journ.*, 1869, i. 394.
(2) Localisation of Function in the Cerebral Hemispheres. *Journ. Mental Science*, Lond., 1868–9, **14**, 454.
(3) The Muscular Sense; its Nature and Cortical Localisation. *Brain*, 1887, **10**, 1.

BAYLISS, W. M. Intravenous Injection of a Gum and Salt Solution in Wound Shock. *Oliver-Sharpey Lectures*, 1918.

BEEVOR, C. The Diagnosis and Localisation of Intracranial Tumours. Lettsomian Lectures. *Trans. Med. Soc.*, Lond., 1907, **30**, 149.

v. BEHRING, with KITASATO, S. Antitoxin for Diphtheria. *Deutsch med. Wochenschrift*, 1890, **16**, 1113, 1145; *ib.*, 1893, **19**, 389, 415.

BENNETT, A. H. Excision of a Tumour from the Brain. *Lancet*, 1884, ii. 1090; also with GODLEE, R. J. *Trans. Med. Chir. Soc.*, Lond., 1885, **50**, 243.

Bernard, Cl. See "Claude Bernard," by Michael Foster in *Masters of Medicine*, Lond., Unwin, 1899.

Bernheim. Experiments on the Relief of Mitral Stenosis. *Johns Hopkins Hosp. Bull.*, 1909, **20**, 107.

Bichat, X. *Anatomie Générale*, 1801.
Œuvres Chirurgicales de Desault, 1798.
Traité des Membranes, 1799–1800.

Bidwell, L. Gastrostomy. *Brit. Med. Journ.*, 1896, ii. 1224.

Bishop, S. Intestinal Suture. *Trans. Med. Chir. Soc.*, Lond., 1887, **70**, 343.

Blondlot. Experimental Gastric Fistula. *Traité Analytique de la Digestion*, Paris, 1843, p. 202.

Blundell, J. *Researches Physiological and Pathological*, Lond., 1824.

Bobbs, J. S. Removal of Gall-stones from the Gall-bladder. *Trans. Indiana Med. Soc.*, Indianopolis, 1868, **18**, 68.

Boothby. Experimental Division and Union of the Abdominal Aorta. *Annals of Surgery*, 1912, **56**, 466.

Bordet, J., et Gengou, O. Researches on Coagulation of the Blood and on Anticoagulant Serums. *Annales de l'Institut Pasteur*, 1901, **15**, 129.

Bouillaud. The Centre in the Brain for Speech. *Arch. Gén. de Méd.*, 1825, **8**, 25.

Bowlby, A. A. *Injuries of Nerves*, Lond., 1889, p. 24.

Boyle, R. Experiments on Respiration.
New Experiments Physio-mechanical touching the Spring of Air, etc., Oxford, 1660; 2nd series, 1669; 3rd series, 1682. Also *Phil. Trans.*, 1670, **5**, 2011, 2035.
Also *Some Considerations touching the Usefulness of Experimental Natural Philosophy*, Oxford, 2nd part, 1671, Essay II. p. 53.

Bradford, J. R. Results following the Experimental Removal of Portions of the Kidney. *Trans. Path. Soc.*, Lond., 1895, **46**, 236.

Broca. The Centre in the Brain for Speech. *Bull. de la Soc. d'Anthropologie*, 1861, **2**, 214; *Bull. de la Soc. Anat.*, 1861–2, **6**, 330; *Gaz. d'Hôp.*, 1864, **37**, 35.

Brunton, L. Experimental Gastric Fistula. *Handbook of the Physiological Laboratory*, 1873, 477, Pl. fig. 311.
On the Possibility of Treating Mitral Stenosis by Surgical Methods. *Lancet*, 1902, i. 352.

Budd, W. Malignant Pustule in England. *Brit. Med. Journ.*, 1863, i. 85.

Bull, W. T. Successful Suture of a Gunshot Wound of the Intestines. *Med. News*, Philadelphia, 1885, **46**, 171.

Burdon-Sanderson, J. Editor of the *Handbook for the Physiological Laboratory*, 1873.

Pathology of Inflammation. Holmes and Halke, *System of Surgery*, 3rd ed., 1883, i. 66.

Cappelen. Suture of a Wound of the Heart. *Brit. Med. Journ.*, 1896, i. ep. 8.

Cardano. Transfusion of Blood. *De rerum varietate*, viii. 4. "Cura Morborum Superstitiosa."

Carle e Rattone. Experimental Production of Tetanus in Rabbits. *Giornale della R. Accad. de Med. di Torrino*, 1884, **32**, 174.

Carrel, A. Experimental Suture and Anastomosis of Arteries, also on Transfusion of Blood. *Lyon Méd.*, 1902, **99**, 114, and many subsequent communications, including *Annals of Surgery*, 1910, **52**, 433.

Chapelier. Prophylactic Injection preventing Tetanus in Horses. *Rec. Méd. Vet.*, 1909, July 15, 437.

Charleton, W. Experiments on Respiration. *Œconomia Animalis*, 1659.

Chauveau. *Nécrobiose et Gangrène*, Paris, 1873.

Chrzonsczewsky. Excretion of Colouring Matter by the Kidneys. *Arch. f. path. Anat.*, 1861, **31**, 153, Taf. viii. ix.; *Cent. f. med. Wissenschaft*, 1863, 756.

Cohnheim, J. Infusion of Normal Salt Solution. *Arch. f. path. Anat.*, 1869, **45**, 338.

Cooper, Astley. Experiments on Ligature of the Carotid and Vertebral Arteries. Panton's MS. Notes of A. C.'s Lectures, 1802–3. *Trans. Med. Chir. Soc.*, Lond., 1809, **1**, pp. 1, 222; *Guy's Hosp. Rep.*, 1836, **1**, 457, 654.

Tying the Aorta. See *The Principles and Practice of Surgery*, ed. by A. Lee, Lond., 1836, p. 228.

Torsion of the Pedicle of a Movable Spleen. *Lectures* (Tyrrell), 1827, iii. 226.

Observations on the Thyroid Gland. *Guy's Hosp. Rep.*, 1836, **1**, 429, 653.

Courten, W. Experiments on Poisons at Montpellier in 1678 and 1679. *Phil. Trans.*, 1712, **27**, 485.

Crile, G. The Direct Transfusion of Blood. *Annals of Surgery*, 1907, **46**, 329.

Cruikshank, W. *The Anatomy of the Absorbing Vessels of the Human Body*, Lond., 1786.

Cushing, H. The Functions of the Pituitary Body. *Am. Journ. Med. Science*, Philadelphia and New York, 1910, **39**, 473.

Czerny, V. Intestinal Suture. *Beitr. z. operative Chiurgie.* Billroth's 25 *Jahr. Doctor's Jubilaum*, 1878, 29.

DAX PÈRE. Speech and the Left Half of the Brain, paper read to the Med. Soc. of Montpellier, 1836, and published *Montpellier Méd.*, 1877, **38**, 233.

DAX FILS. *Gaz. hebdom.*, 1865, 2 sér., **2**, 259.

DEL VECCHIO, S. Experimental Suture of Heart Wounds. *Atti* di xi. *Cong. Med. internaz.*, 1894, Roma; 1895, iv. 297.

DIEUDONNÉ. Prophylactic Injection Preventing Tetanus in Horses. *Rec. Méd. Vet.*, 1909, July 15, 433; and *Bull. Institut Pasteur*, 1909, 855.

DUDGEON, L. S., and SARGENT, P. Bacteriology of Peritonitis. *Erasmus Wilson Lectures*, 1905.

DURANTE. Tumour of Dura Mater Removed. *Trans. IX. Internat. Congress*, Lond., 1881, i. 570.

ECK (EKK), N. V. Experimental Anastomosis between the Portal Vein and Inferior Vena Cava. *Militar Med. Journ.*, 1877.

EDMUNDS, J. Cæsarean Section. *Lancet*, 1861, i. 4; *ib.*, 1876, ii. 818.

EHRLICH, P. *The Treatment of Syphilis with Dioxydiamidoarsenobenzol*, Rebman, Lond., 1911.

v. EISELSBERG. Suture of Wound of Pulmonary Artery *Arch. f. klin. Chir.*, 1909, **89**, 757.

ERICHSEN, J. *Science and Art of Surgery*, 8th ed., edited by M. Beck, 1884, i. 2.

FEHLEISEN, F. Erysipelas Micro-organisms. *Deutsch Zeitschrift f. Chir.*, 1882, **16**, 391, Taf. v, vi.

FERGUSSON, J. Removal of a Prolapsed Spleen. *Phil. Trans.*, 1738, **40**, 425.

FERRIER, D. Experimental Researches in Cerebral Physiology and Pathology. *The West Riding Lunatic Asylum's Medical Reports*, 1873, 30.

The Functions of the Brain, 1876, 2nd ed., 1886.

and TURNER, W. A. Experiments on Monkeys regarding the Functions of the Cerebellum. *Brain*, 1893, **16**, 1.

FLOURENS. *Recherches Expérimentales sur les propriétés et les fonctions du Système Nerveux dans les Animaux Vertébrés*, Paris, 1824, 2^{me} ed., 1842.

FOX, E. J. Thyroid Extract Administered by the Mouth. *Brit. Med. Journ.*, 1892, ii. 941.

FREER, G. *Observations on Aneurysm*, Birmingham, 1807.

FREYER, P. J. A Case of Hydrophobia Eighteen Months after Infection. *Brit. Med. Journ.*, 1919, i. 795.

FRIEDRICH, P. L. Experimental Excision of Septic Wounds. *Arch. f. klin. Chir.*, 1898, **57**, 288.

FRITSCH, G., u. HITZIG, E. Electrical Excitation of the Brains of Dogs. *Arch. f. Anat. Physiol.*, etc., 1870, 300.

GALEN. *Opera Omnia*, Kühn, 1821, 33.
Also SIMON, M. *Sieben Bücher Anatomie des Galen*, Leipzig, 1906.
MEYER, STEINEG. Studien zur Physiologie des Galenos. *Arch. f. Gesch. d. Med.*, 1911, **5**, 172.
MILNE. Galen's Knowledge of Muscular Anatomy. *XVII. Internat. Congr. Med.*, History of Medicine Section, p. 389.
GASTON. Experimental Cholecystenterostomy. *Atlanta Med. and Surg. Journ.*, 1884–5, ns. **1**, 336; *Med. News*, Phila., 1892, **60**, 651.
GÉLY. *Recherches sur l'emploi d'un Nouveau procédé de Nature contre les divisions de l'intestin*, etc., Nantes, 1844. Tract in the Library of the Royal Society of Medicine of London.
GOLTZ, F. L. The Decerebrate Dog. *Arch. f. Ges. Physiol.*, 1892, **51**, 570, Taf. xii.; *ib.*, 1896, **63**, 362.
GREEN, T. A. Heart Massage as a means of Restoration in Cases of Apparent Sudden Death. *Lancet*, 1906, ii. 1708.
GROSS, S. D. *An Experimental Critical Inquiry into the Nature and Treatment of Wounds of the Intestine*, Louisville, Ky., 1843.
GULL, W. W. On a Cretinoid State Supervening in Adult Life in Women. *Trans. med. Chir. Soc.*, Lond., 1874, **7**, 180.
GUSSENBAUER, C., u. v. WINIWARTER, A. Experimental Excision of Part of the Stomach in Dogs. *Arch. f. klin. Chir.*, 1876, **19**, 347.

HALDANE, J. C. Researches on the Air in Mines, etc. *Journ. of Path. and Bact.*, 1892, **1**, 174; (with LORRAINE SMITH) *Journ. of Physiology*, 1897, **18**, 295.
HALL. Experiments on the Bite of Virginian Rattlesnakes. *Phil. Trans.*, 1728, **35**, 309.
HALL, MARSHALL. *Asphyxia; its Nature and its Remedy.* Lond., 1856.
v. HALLER, A. *Elementa Physiologiæ*, Lausanne, 1759–66.
Opuscula pathologica, Lausanne, 1553.
Bibliotheca Chirurgica, Bern, 1774–77.
Disputationum Chirurgicarum Selectarum Collectio, Lausanne, 1755, xxvi.
HALSTED, W. S. The Submucous Coat of the Intestines. *Am. Journ. Med. Sciences*, 1887, **94**, 436.
HAMANN, C. A. Ligature of the Abdominal Aorta, *Annals of Surgery*, 1916, **68**, 217.

HEAD, H., and SHERREN, J. The Consequences of Injury to the Peripheral Nerves in Man. *Brain*, 1905, Summer Number, 116.

HEIDENHAIN, R. P. H. Excretion of Colouring Matter by the Kidneys. *Arch. f. Ges. Physiol.*, 1875, **9**, 26.

HERLIN. Experiments on Opening and Excising the Gall Bladder in Dogs and Cats. *Journ. de Méd. Chir. Pharm.*, 1767, **27**, 463.

HEWSON, W. A Description of the Lymphatic System in Man. *Experimental Inquiries*, Part II, 1774.

HILL, L. *The Cerebral Circulation*, 1896.

Blood-vessels and Pressure, *Lancet*, 1920, i. 359.

HOOKE, R. His Experiment of Keeping the Lung Inflated. *Phil. Trans.*, 1667, **2**, 539.

HOPPE, F. The Action of Carbon Monoxide Gas on Hæmoglobin. *Arch. f. path. Anat.*, 1857, **11**, 288; *ib.*, 1858, **13**, 104; *ib.*, 1862, **23**, 446.

HORSLEY, V. On the Thyroid Gland. *Proc. Roy. Soc.*, 1884.

Report of the Committee on Myxœdema. *Trans. Clin. Soc.*, Lond., 1888, **21**, supplement.

The Functions of the Thyroid Gland. Virchow's *Festschrift*, 1891, i. 369.

The Prevention of Embolism following Mastoid Suppuration. *Trans. Clin. Soc.*, Lond., 1885, **19**, 290.

Brain Surgery. *Brit. Med. Journ.*, 1886, i. 670, ii. 346; *ib.*, 1887, i. 863.

On Epilepsy. *Lancet*, 1886, ii. 1211; *Brit. Med. Journ.*, 1892, i. 693.

and FERRIER, D. Cerebral Abscess. *Trans. Med. Soc.*, Lond., 1888, **11**, 233.

and BEEVOR. Experiments on the Brain of Monkeys. *Phil. Trans.*, 1887, **178**, 153; *ib.*, 1889, **179**, 205; *ib.*, 1894, **185**, 39.

and CLARKE. Experiments on the Cerebellum. *Brain*, 1905, **28**, 13; *ib.*, 1908, **31**, 138.

and GOWERS, W. Removal of a Spinal Cord Tumour. *Trans. Med. Chir. Soc.*, Lond., 1888, **63**, 377.

HUGUIER. Prophylactic Injection Preventing Tetanus in Horses. *Rec. Méd. Vet.*, 1909, June 15, 356.

HUNTER, J. *Works* (Palmer). 4 vols., 1835.

HUNTER, W. *Medical Commentaries*, Part I, 1762.

HUTCHINSON, J. On Intestinal Obstruction. *Brit. Med. Journ.*, 1878, ii. 305.

JACKSON, HUGHLINGS. Remarks on the Evolution and Dissolution of the Nervous System. *Journ. of Mental Science*, 1888, **33**, 125.

JOBERT. Intestinal Suture. *Arch. Gén. de Méd.*, 1824, **4**, 71; also *Mémoire sur les plaies du Canal intestinal*, 1827; *Traité des Maladies Chirurgicales*, Paris, 1829.

JOLYET et LAFFOND. Intravenous Saline Infusion. *Gaz. Med. de Paris*, 1879, 101.

JONES, J. F. D. *A Treatise on the Process Employed by Nature in Suppressing the Hæmorrhage, and on the use of the Ligature*, Lond., 1805.

JONES, S. Gastrostomy. *Lancet*, 1866, ii. 665.

KADER, B. Gastrostomy. *Centralblatt f. Chir.*, 1896, **23**, 665.

KEYSER. Cæsarean Section. *Arch. f. Gynekol.*, 1882, **19**, 177.

KIMPTON and BROWN. Transfusion of Blood by mixing with Sodium Citrate. *Journ. Am. Med. Ass.*, 1913, **61**, 117.

KITASATO, S. Tetanus Bacilli. *Arch. f. klin. Chir.*, 1889, **39**, 423.

KLEBS, E. *Beiträge zur path. Anat. der Schusswunden*, 1872.

KOCH, R. *Untersuchungen über die Ætiologie des Wundinfektions Krankheiten*, Leipzig, 1878.

KOCHER, T. Excision of Goitre and its Results. *Centralblatt f. Chir.*, 1883; Kong. Beil., 23, 29; *Arch. f. klin. Chir.*, 1883, **29**, 254.

On Concussion, Compression and Surgical Interference in Brain Affections. Nothnagel's *Specielle Pathologie und Therapie*, Wien, 1901, Bd. ix., iii. Theil, ii. Abtheilung.

KÖRTE, W., u. BERNHARD, M. Faciohypoglossal Anastomosis. *Deutsch med. Wochenschrift*, 1903, **29**, 293.

KRAUSE, R., with BELTRAMI, PENNA and CUENCA. The Efficiency of Normal Serum in Anthrax Infections and for Human Anthrax. *Wien klin. Wochenschrift*, 1917, **30**, 553, 566.

KRONECKER u. SANDER. Experiments on the Infusion of Normal Salt Solution in Dogs. *Berl. klin. Wochenschrift*, 1879, 767.

KRUGER. Removal of a Pulmonary Embolus. *Zentralblatt f. Chir.*, 1909, **36**, 757.

LANCISI. Experimental Ligature of Arteries in Continuity in his *De Aneurysmatibus*, 1728, Proposition xxxviii.

LANDSTEINER, R. Phenomena of Agglutination in Normal Human Blood. *Wien Klin. Wochenschrift*, 1901, 1132.

LANE, W. A. Suppuration in the Lateral Sinus. *Trans. Clin. Soc.*, Lond., 1888, **22**, 255.

LANGENBUCH, C. Excision of the Gall-bladder. *Berl. klin. Wochenschrift*, 1882, **19**, 725.

Lawrence, W. Cases of Cutaneous Anthrax in London. See South's Translation with Notes of *A System of Surgery*, by J. M. Chelius, 1847, i. 64.

Legallois. The Centre for Respiration in the Medulla. *Œuvres*, 1830, T. i.

Lembert. Intestinal Suture. *Repertoire gén. de l'Anat. et de Physiol.*, 1826, **2**, Pl. V; also *Arch. Gén. de Méd.*, 1827, **13**, 234.

Leroy d'Etiolles. Rapport par Magendie—On the Inflation of the Lungs as an Aid to those who have been Submerged or Asphyxiated. *Journ. de Physiologie*, 1829, **9**, 97.

Libavius. On Transfusion, in *Chirurgia Transfusoria, Appendix Necessaria Syntagmatis Areanorum Chymicorum*, Erfurt, 1615. Also *Defensio Syntagmatis Areanorum Chymicorum Contra Henningum Scheunemannum*, Frankfurt, 1615.

Lindemann, E. Transfusion of Blood with a Syringe. *Am. Journ. Dis. of Children*, 1913, **6**, 28.

Lister, J. *Collected Papers*, 1909, and *Life*, by Sir R. Godlee.

Lœffler, F. The Bacillus of Diphtheria. *Mitth. a. a. k. Gesundheitsamt*, 1884, **2**, 421.

Louis, M. Experiments on Drowning. *Mém. de l'Acad. de Chir.*, 1768, **4**, 455, 513.

Lower, R. Transfusion of Blood. *Phil Trans.*, 1666, **1**, 353, 392; *ib.*, 1667, **2**, 557. *Tractatus de transfusione sanguinis*, Lond., 1669.

Luciani, L. Experiments on the Physiology of the Cerebellum. *Linie Generali della fisiologia del Cervelletto*, translation in *Alienist and Neurologist*, St. Louis, 1885, **6**, 339. *Arch. ital. de biol.*, Turin, 1895, **23**, 217.

Macewen, W. Surgery of the Spinal Cord and Brain. *Glasgow Med. Journ.*, 1884, **21**, 142; *Brit. Med. Journ.*, 1888, ii. 302.

Mackenzie, H. Myxœdema treated by Feeding with fresh Thyroid Glands. *Brit. Med. Journ.*, 1892, ii. 940.

Madden and Mortimer. Poisoning by Decoction of Laurel Leaves. *Phil. Trans.*, 1731, **37**, 84, 187.

Magendie, F. Experiments on the Functions of the Spinal Nerve Roots. *Journ. de Physiologie*, 1822, **2**, 276, 366.

Maissoneuve. Experiments and Operations on Intestinal Anastomosis. *Arch. Gén. de Méd.*, 1844, 4 sér., **6**, 174; *Bull. de la Soc. de Chir.*, 1854, **4**, 381; *Clinique Chirurgicale*, Paris, 1864, 488.

Marie. On the Speech Centre. *La Semaine Méd.*, 1906, 244, 492, 555.

On Acromegaly. *Rev. de Méd.*, 1886, **6**, 297; *ib.* (with Marinesco, G.). *Arch. de Méd. Expér. et d'Anat. path.*, **3**, 539.

Mayo, H. Experiments distinguishing Motor Cranial Nerves, *Anatomical and Physiological. Commentaries*, No. i, Aug. 1822, No. ii, July 1823.

Mayow, J. Experiments on the Blood and its Oxidation in *Tractatus duo*, Oxford, 1668, and *Tractatus quinque*, Oxford, 1669.

Meltzer and Auer. Intratracheal Insufflation Experiments. *Journ. of Exp. Med.*, 1909, **11**, 622; *ib.*, 1911, **14**, 569.

Annals of Surgery, 1910, **52**, 716.

Merrem, D. Experiments on the Excision of the Pylorus in Dogs. *Animadversiones quædam Chirurgiæ Experimentis in Animalibus factis*, illustratæ auctore, Gissæ, 1810.

Meyer, W. Experimental Excision of Part of a Lung. *Journ. Am. Med. Ass.*, 1909, **53**, 1978.

Metchnikoff with Roux. Inoculation of Syphilis into Anthropoid Apes. *Bull. de l'Acad. de Méd.*, 1903, **50**, 101.

Miakowski, u. v. Mering. Removal of the Pancreas from Dogs. *Arch. f. Exp. Path. u. Pharm.*, 1889. **26**, 271.

Mikulicz. Closure by Suture of Perforated Gastric Ulcers. *Cent. f. Chir.*, 1884, 754, and Volkmann's, *Sammlung klin. Vorträge*, No. 262.

Milligan, W. Treatment of Cerebellar Abscess following Ear Disease. *Brit. Med. Journ.*, 1890, i. 231 (with A. W. Hare); also *ib.*, 1914, ii. 833.

Molinelli. On Brachial Aneurysms. *Comment. Boniensi Scient. et Artium*, 1745, ii. Part I, p. 178.

Morand, S. F. Experiments on the Ligature of Arteries. *Mém. de l'Acad. des Sciences*, 1736.

On Abscess of the Brain. *Opuscules de Chirurgæ*, 1768.

Morgagni. On Hæmorrhage into the Pericardium Compressing the Heart. *De Sedibus et Causis Morborum*, Ep. xxvi. 18, 26, 27, 28, etc.

Mosler. Experimental Excision of the Spleen and its Results. *Centralblatt f. d. med. Wissenschaft*, 1871, **9**, 290.

Moss, W. L. Studies on Isoagglutins and Isohæmolysins. *Johns Hopkins Hospital Bull.*, 1910, **21**, 63; *ib.*, 1911, **22**, 238.

Murphy, J. B. Intestinal Anastomosis. *Med. Record*, 1892, **42**, 665; *ib.*, 1894, **45**, 651.

Med. News, Philadelphia, 1895, **67**, 533, 569.

Continuous Rectal Infusion. See The Treatment of Diffuse Septic Peritonitis. Le Conte, *Annals of Surgery*, 1906, **43**, 231.

MURRAY, G. Myxœdema treated with Thyroid Juice. *Brit. Med. Journ.*, 1891, ii. 796; *ib.*, 1892, ii. 449.

NEUBER, G. The Aseptic Treatment of Wounds. See *Die Aseptische Wundbehandlung in mein Chir-privathospitalern in Kiel,* 1886. Also *Arch. f. klin. Chir.*, 1892, **44,** 438.

NICOLAIER. Tetanus Infection. *Deutsch med. Wochenschrift,* 1884, **10,** 824.

NOURSE, E. The Case of a Lad Bitten by a Mad Dog Dying of Hydrophobia after Nineteen Months. *Phil. Trans.*, 1738, **40,** 5.

OLDENBURG, H. An Account of the Rise and Attempts of a Way to conveigh Liquors immediately into the Mass of Blood. *Phil. Trans.*, 1666, **1,** 128.

OPIE, E. L. Experiments on the Production of Hæmorrhagic Pancreatitis. *Johns Hopkins Hosp. Bull.*, 1901, **12,** 182.

ORD, W. On Myxœdema. *Trans. Med. Chir. Soc.*, Lond., 1878, **61,** 57.

PAGET, J., with SAVORY, W. Experimental Division of the Tendo Achillis. See Paget's *Lectures on Surgical Pathology,* 3rd ed. (W. Turner), 1870, 199.

PANUM, P. L. The Catalytic Theory of Septicæmia. *Arch. f. path. Anat.* (Virchow), 1874, **60,** 283.

PARKES, C. T. Experimental Gunshot Wounds of the Intestines in Dogs. *Journ. Am. Med. Ass.*, 1884, **2,** 589.

PASTEUR—

The Life of Pasteur, by René Vallery-Radot, trans. by Mrs. Devonshire, with a Foreword by Sir W. Osler, 1911. 2 vols.

On Anthrax. *Bull. Acad. de Méd.*, 1877, 2 sér., **6,** 781; 1879, 2 sér., **8,** 1063.

On Rabies and Hydrophobia, with CHAMBERLAND, ROUX and THUILLIER. *C. R. Acad. des Sciences,* 1881, **92,** 159, 1259; *ib.*, 1884, **98,** 457.

Bull. Acad. de Méd., 1882, 2 sér., **11,** 1440; *ib.*, **13,** 337.

Traitement de la Rage, Paris, 1886.

PETERSEN, W. Gastroenterostomy. *Internat. Med. Cong.*, Paris, 1900. See *Arch. f. klin. Chir.*, 1900, **62,** 94; *Beitr. z. klin. Chir.*, 1901, **29,** 597.

PETIT, J. L. On the Ligature of Arteries. *Mém. de l'Acad. des Sciences,* 1731, 1732, 1733, 1735.

On Trephining. *Mém. de l'Acad. de Chir.*, 1744, **1**; *Traité des Maladies Chir.*, T. i.

PITTS, B., and BALLANCE, C. Three Cases of Splenectomy for Rupture of the Spleen. *Trans. Clin. Soc.*, Lond., 1896, **29**, 77.

POTT. On Injuries to the Head *Works* (Earle), 1808, i. 1.

PROCHASKA. Idea of the Action of the Nervous System. *Annotationes Academiæ*, 1784, Fasc. iii.

RANBY, P. A Case of Hysterical Hydrophobia. *Phil. Trans.*, 1747, **44**, 240.

REDI, FR. The Poison of Vipers. *Phil. Trans.*, 1666, **1**, 160.

REVERDIN, J. L., and REVERDIN, A. Myxœdema following Operations for Goitre. *Rev. Méd. de la Suisse Romande*, 1883, **3**, 169, etc., etc.

REHN. Successful Suture of a Wound of the Heart Muscle. *Centralblatt, f. Chir.*, 1896, 1048.

RICHARDSON, B. W. Experimental Suture of the Abdominal Wall. *Nature*, 1876, **14**, 151.

Suspended Animation. *Nature*, 1879, **20**, 107.

RICHARDSON, W. G. Tetanus due to Infected Catgut Ligatures. *Brit. Med. Journ.*, 1909, i. 967, 1481.

RICHET, A. The Recovery of Sensation after Division and Reunion of Nerves. *C. R. Acad. des Sciences*, 1875, **81**, 217.

RIEGNER. Excision of a Ruptured Spleen. *Berl. klin. Wochenschrift*, 1893, **30**, 177.

RINGER, S. The Addition of Minute Amounts of Calcium Salts to the Normal Salt Solution. *Journ. of Physiology*, 1883–4, **4**, 29, 222.

ROSENBACH. The Bacilli Causing Tetanus. *Arch. f. klin. Chir.*, 1886, **34**, 306.

ROSENTHAL. On Apnœa. See *Ueber die Athmungsbewegung und ihre Beziehungen zum Nervus Vagus*, 1862.

ROUX et YERSIN. Diphtheria Antitoxin. *Annales de l'Institut Pasteur*, 1888, 2, 629; *ib.*, 1889, **3**, 273.

ROWNTREE, L. G., and GERACHTY, T. J. Excretion by the Kidneys of the Colouring Matter Phenolsulphonephthalein. *Journ. of Pharm. and Exp. Therap.*, 1909, **1**, 579.

RUSSELL, RISIEN. On the Functions of the Cerebellum. *Phil. Trans.*, 1895, **185**, 819.

SALMONI. Experimental Suture of Wounds of the Heart made in Dogs. *Centralblatt f. Chir.*, 1896, 1224.

SANGER. Cæsarean Section. *Der Kaiserschnitt bei Uterus Fibromen*, Leipzig, 1882.

SAPORTA. An Early Reference to Anthrax in Man. See his *De tumoribus præter Naturam*, Lugduni, 1624, i. 15.

SAUCEROTE. Experiments regarding Contre Coup in Head Injuries. *Mém. pour les prix de l'Acad. roy. de Chir.*, 1732.

SCARPA. On the Ligature of Arteries in his *Sull' Aneurisma*, Pavia, 1804; and *Append. Sull' Aneurisma*, 1817.

SCHAFER, E. A. Experiments on Artificial Respiration in Cases of Drowning. *Trans. Med. Chir. Soc.*, Lond., 1904, **87**, 609.

On the Visual Centre in the Brain. *Brain*, 1889, **11**, 1, 145.

with HORSLEY, V. Experiments on the Functions of the Cerebral Cortex. *Phil. Trans.*, 1889, 179, 1.

SCHAUDINN, F., u. HOFFMANN, E. The Spirochæte Pallida Causing Syphilis. *Arb. a. d. Gesundheitsamt*, Berlin, 1905, **22**, 527.

SCHIFF, M. Experimental Removal of the Thyroid Gland and Subsequent Thyroid Grafting. *Rev. de la Suisse Romande*, 1884, **4**, 65, 425.

The Heart Restarted by Rhythmical Squeezing. *Recueil des Mémoires Physiologiques*, 1874, Vol. 3.

SCHIMMELBUSCH. Aseptic Treatment of Wounds. Eng. trans. by Dr. Rake, 1894.

SCLAVO. A Specific Serum against Anthrax from the Ass. *Centralblatt f. Bakt. v. Parasit*, 1. abth., 1895, **18**, 744.

SEDILLOT. Gastrostomy. *Gaz. Méd.*, 1846, 600, etc.; *ib.*, 1847, 7, etc.; *ib.*, 1849, 989.

SENN, E. J. Gastrostomy. *Journ. Am. Med. Ass.*, 1896, **27**, 1142.

SENN, N. *The Surgery of the Pancreas.* Philadelphia, 1886.

Experiments on and Treatment of Intestinal Obstruction *Journ. Am. Med. Ass.* 1888, **10**, 767, 807.

Annals of Surgery, 1888, **7**, 1, etc.

Intestinal Surgery, Chicago, 1889.

SHERRINGTON, C. Experiments on the Function of the Cerebellum. See his *The Integrative Action of the Nervous System*, Lond., 1906.

with GRÜNBAUM, A. S. F. Localisation in the Motor Cortex of the Anthropoid Ape. *Trans. Path. Soc.*, Lond., 1902, **53**, 127.

SHIPTON, J. Excision of a Piece of the Intestine of a Dog. *Phil. Trans.*, 1703, **22**, 1.

SIMON, G. *Die Extirpation der Milz am Menschen*, Giessen, 1857; *Chirurgie der Nieren*, Erlangen, 1871.

SPENCER, W. G. Death of a Child from Hydrophobia two years and four months after being Bitten by a Rabid Dog. *Brit. Med. Journ.*, 1891, i. 277.

SPENCER, W. G., and HORSLEY, V. Changes produced in the Circulation and Respiration by Increase of the Intracranial Pressure or Tension. *Phil. Trans.*, 1891, **182**, 201.

STAMM, M. Experimental Gastrostomy. *Med. News*, Philadelphia, 1894, **65**, 324.

STARR. The Account of a Horse bit by a Mad Dog. *Phil. Trans.*, 1750, **46**, 474.

TETANUS Prophylaxis on July 4 in U.S.A. See Editorial Special Article. *Journ. Am. Med. Ass.*, 1907, **49**, 685.

TOOTH, H. Five hundred Cases of Cerebral Tumour at the National Hospital, Queen Square, 1902–11. *Proc. Roy. Soc. Med.*, Lond., 1912–13, **6**, Neurological Sect. 1

TRAVERS, B. *Inquiry into the Process of Nature in Repairing Injuries of the Intestines*, Lond., 1812. See also Holmes and Hulke, *System of Surgery*, 3rd ed., 1883, i. 893.

TRENDELENBURG. Experiments on and Operations for the Removal of an Embolus from the Pulmonary Artery *Arch. f. klin. Chir.*, 1908, **86**, 686.

TROUSSEAU. Tracheotomy for Diphtheria. *Clinique Médicale*, 1868, i. 416.

VALSALVA. Ligature of Arteries. *Opera* (Morgagni), Ep. 13, p. 507.

VERNEUIL. Gastrostomy for Fibrous Stricture of the Œsophagus. *Bull. Acad. de Méd.*, 1876, 2^{me} sér., **5**, 1023.

Tetanus in Old Horses. *Gaz. hebdom.*, 1886, **23**, 597, etc.; *ib.*, 1887, **24**, 117; *ib.*, 1890, **27**, 561.

Rev. de Chir., 1887, **7**, 757, 949; *ib.*, 1888, **8**, 169, 639.

VESALIUS. *De humani corporis fabrica*, 1543, vii. 19, p. 658; *ib.*, 1555, vii. 19, p. 818; *ib.* (Boerhaave et Albinus), i. 567.

VOELEKER, F., u. JOSEPH, E. Excretion of Indigocarmine by the Kidneys. *Deutsch Med. Wochenschrift*, 1904, **30**, 536.

WALSHAM, W. J. Is Trephining the Skull a Dangerous Operation *per se ? St. Bart.'s Hosp. Rep.*, 1882, **18**, 213.

WASSERMANN, A. The Serodiagnosis of Syphilis. *Berl. klin. Wochenschrift*, 1907, **15**, 99.

WELLS, S. Suture of the Abdominal Wall in his *Ovarian and Uterine Tumours*, Lond., 1882, 197.

WÖLFLER, A. Gastroenterostomie. *Centralblatt f. Chir.*, 1881, **8**, 705.

Ueber die von Herren Billroth, Ausgeführten Resektionem des Karcinomatösen Pylorus, Wien, 1881.

WOOLSEY. Recovery after the Closure of Sixteen Wounds of the Intestines. *Annals of Surgery*, 1896, **23**, 422.
WRIGHT, A. E. A New Method of Blood Transfusion. *Brit. Med. Journ.*, 1891, ii. 1202.

ZAMBECCARI, J. Experimental Excision of Abdominal Viscera in a Letter to Redi. See Le Clerc et Manget (Clericus et Mangetus), *Bibliotheca Anatomica*, Geneva, 1699, ii. 1202.

Printed in Great Britain for the UNIVERSITY OF LONDON PRESS, Ltd.
by RICHARD CLAY & SONS, Ltd., London and Bungay.

BINDING SECT. AUG 7 1979

PLEASE DO NOT REMOVE
CARDS OR SLIPS FROM THIS POCKET

UNIVERSITY OF TORONTO LIBRARY

RD Spencer, Walter George
29 Animal experiments and
S64 surgery

BioMed.

87